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plicants: SANKYO COMPANY, LIMITED [JP/JP]; 5–1, Nihonbashi–Honcho 3–chome, Chuo–ku, Tokyo 103 (JP). GLYCOMED INCORPORATED [US/US]; 9393 Towne Centre Drive, San Diego, CA 92121 (US).

ventors: SATO, Susumu; Sankyo Company, Limited, 2–58, Hiromachi 1–chome, Shinagawa–ku, Tokyo 140 (JP). KURIBAYASHI, Takeshi; Sankyo Company, Limited, 2–58, Hiromachi 1–chome, Shinagawa–ku, Tokyo 140 (JP). USHIYAMA, Shigeru; Sankyo Company, Limited, 2–58, Hiromachi 1–chome, Shinagawa–ku, Tokyo 140 (JP). YASUMOTO, Takashi; Sankyo Company, Limited, 2–58, Hiromachi 1–chome, Shinagawa–ku, Tokyo 140 (JP). TANZAWA, Kazuhiko; Sankyo Company, Limited, 2–58, Hiromachi 1–chome, Shinagawa–ku, Tokyo 140 (JP). TAKAHASHI, Masaaki; Sankyo Company, Limited, 2–58, Hiromachi 1–chome, Shinagawa–ku, Tokyo 140 (JP).

(74) Agents: WOLFF, Jessica, R. et al.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071–2066 (US).

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tle: ARYL C-GLYCOSIDE COMPOUNDS AND SULFATED ESTERS THEREOF

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α or β bond or a disaccha-
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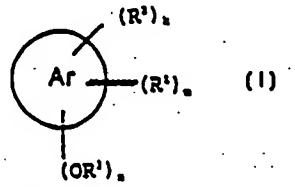

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aryl C–glycoside can be used in the treatment or prevention of inflammatory diseases, autoimmune diseases, infections, cancer and metastasis, reperfusion disorders, thrombosis, ulcer, wounds and osteoporosis.

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DESCRIPTION

Aryl C-Glycoside Compounds And Sulfated Esters Thereof

Field of the Invention

The present invention provides a series of aryl C-glycoside compounds in the form of chemically and physiologically stable glycomimics of glycoepitopes that can serve as the active center of polysaccharides which govern various intercellular actions, interactions between cells and interstitial tissue (cell differentiation and growth, recognition and adhesion, fertilization and implantation, canceration, immunity and aging) and receptor functions (with respect to hormones, toxins, bacteria and viruses), sulfated forms thereof, pharmacologically acceptable salts thereof and preparations containing the same.

More particularly, the present invention provides a series of aryl C-glycoside compounds in the form of chemically and physiologically stable glycomimics that may inhibit interactions between cells and between cells and interstitial tissue mediated by glycosides, sulfated esters thereof, pharmacologically acceptable salts thereof and preparations containing the same, which can be used in the treatment and/or prevention of inflammatory diseases, autoimmune diseases, infections, cancer and cancer metastasis, reperfusion disorders, thrombosis, ulcer, wounds, osteoporosis and other selective-mediated disorders.

The compounds of the present invention can preferably bind to E, L and P-selectin.

Background Of The Invention

Sugar chains are located on the cell surface in the form of constituents of glycolipids or glycoproteins, or in the extracellular matrix (interstitial tissue) in the form of

constituents of proteoglycans, and are known to function as receptors of various hormones (bFGF, tPA, erythropoietin, renin, etc.), toxins (cholera toxin, tetanus toxin, botulinus toxin, chlostridium toxin, Shiga toxin, enteritis vibriosis heat-resistant toxin, etc.), bacteria (colibacillus, pneumococcus, staphylococcus, actinomycetes, gonococcus, pseudomonas, etc.), and viruses (influenza virus, Sendai virus, Newcastle virus, hepatitis B virus, polio virus, AIDS virus, etc.). Many sugar claims are also deeply involved in the basic phenomena of multicellular society, including cell differentiation, and growth, recognition and adhesion, fertilization and implantation, canceration, immunity, aging and so forth, through intracellular actions and interactions between cells and interstitial tissue.

At present, due to the tremendous progress of instrumental analysis technology, the structures of numerous glycoepitopes that serve as the active centers of sugar chains governing such interactions and receptor functions are being analyzed and elucidated. As an example of this, the following list provides the structures of sugar chains involved in these interactions and functions:

(1) Receptor sugar chains of host cells with respect to bacteria
(2) Receptor glycolipids to which toxins bond
(3) Receptor sugar chains to which viruses bond
(4) Receptor sugar chains of cellular adhesive molecules (selectin)
(5) Sugar chains functioning as tumor markers that appear in various cancer cells.

Glycoreceptors for viruses, bacteria, toxins and carcinoma metastasis are discussed in the following publications:

Glycoreceptors for viruses: Paulson J.C., The Receptors, Vol. II, edited by Conn, P.M. Academic Press, (1985), 131

Glycoreceptors for bacteria: Stromberg et al., EMBO J., (1990), 9, 2001

Glycoreceptors for toxins: Karsson et al., Sourcebook of Bacterial Protein Toxins, edited by Alouf, J.E., Freer J.H., Academic Press, (1990), 56, 3537; T. Tamaya, Mebio (1993), 10(5), 26; and Y. Tanaka, Mebio, (1993), 10(5), 56

Glycoreceptors for carcinoma metastasis: H. Komazawa, M. Kojima, Y. Igarashi, I. Saiki, Mebio, (1993), 10(5), 99

Inhibitors of these interactions and receptor functions are expected to be effective therapeutic and preventive agents against each of the diseases to which these are related or against each of the diseases that occur in cases in which these interactions and receptor functions have become excessive or abnormal.

Examples of related diseases include acute or chronic inflammatory diseases such as rheumatoid arthritis, asthma, allergy, psoriasis and septic shock, or transplanted tissue rejection reactions, reperfusion disorders, adult dyspnea syndrome, ischemia, ulcerative colitis, atherosclerosis, thrombosis, ulcer, infections, cancer and cancer metastasis, wounds and osteoporosis (see Mulligan, M.S., et al., Nature, (1993), 364, 149; Mulligan, M.S., et al., J. Exio. Med., (1993), 178, 623; Lefer, D.J., et al., Circulation, (1994), 90, 2390; Bevilacque, M.P., et al., J. Clin. Invest., (1993), 91, 379; Lee M., Med. Sci. Res., (1992), 20, 539; Erbe, D.V., et al., J. Cell Biol., (1993), 120, 1227; Stahl, W., et al., Chem. Int. Ed. Engl., (1994), 33, 2096; Sprengard, U., et al., Angew Chem., (1995), 107, 1104; Kojima, N., et al., Biophys. Res. Commun., (1992), 182, 1288; Ichikawa, Y., et al., Chem. In Brit., (1994), 117; Buerke, M., et al., J. Clin. Invest., (1994), 1140; and Han, K.T., et al., J. Immunology, (1995), 155, 4011).

As it has become clearer that sugar chain derivatives are closely related to these diseases, synthesis of numerous sugar

chain derivatives has been attempted for the purpose of developing new and effective pharmaceuticals having different modes of action from those in the past. As an example of this, chemical, enzymatic and chemo-enzymatic synthesis of sialyl Lewis X (sLe^x) and its derivatives, a terminal tetrasaccharide of membrane glycolipids and glycoproteins, which has been identified as a native ligand for the E-, L-, P-selectins (adhesion molecules) have been discussed in the following publications:

Chemical Syntheses:

1) Sato, S., et al., Tetrahedron Lett., (1988), 29, 5267
2) Tyrell, D., et al., Proc. Natl. Acad. Sci. USA, (1991), 88, 10372
3) Zimmerman, P., et al., Tetrahedron Lett., (1990), 31, 1849
4) Nicolaou, K.C., et al., J. Am. Chem. Soc., (1990), 12, 3693
5) Kameyama, A., et al., Carbohydr. Res., (1990), 200 269
6) Bommer, R., et al., Liebigs Ann. Chem., (1991), 425
7) Nilsson, S., et al., J. Carbohydr. Chem., (1991), 10, 1023
8) Nicolaou, K.C., et al., J. Am. Chem. Soc., (1993), 115; 8843
9) Danishefsky, S.J., et al., J. Am. Chem. Soc., (1992), 114, 8331
10) Dannishefsky, S.J., et al., J. Am. Chem. Soc., (1995), 117, 1940
11) Nashed, M.N., et al., Carbohydr. Res., (1993), 250, c1-c4
12) Brandley, B.K., et al., Glycobiology, (1993), 3, 633
13) Sprengard, U., et al., Angnew. Chem. Int. Ed. Engl., (1995), 34, 990

14) Kretzschmar, G., et al., Tetrahedron, (1995), 51, 13015

15) Kiso, M., et al., J. Carbohydr. Chem., (1993), 12, 673.

Enzymatic Syntheses:

(1) DeFrees, S.A., et al., J. Am. Chem. Soc., (1993), 115, 7549

(2) Sabesan, S., et al., J. Am. Chem. Soc., (1986), 108, 2068

(3) Toone, E.J., et al., Tetrahedron, (1989), 45, 5365

(4) David, S., et al., Adv. Carbohydr. Chem. Biochem., (1991), 49, 175

(5) Ichikawa, Y., et al., Anal. Biochem., (1992), 114, 5452

(6) Ichikawa, Y., et al., Am. Chem. Soc., (1991), 113, 4698

(7) Ichikawa, Y., et al., J. Am. Chem. Soc., (1991), 113, 6300

Chemo-Enzymatic Synthesis:

(1) Ichikawa, Y., et al., J. Am. Chem. Soc., (1992), 114, 9283

(2) Schuster, M., et al., J. Am. Chem. Soc., (1994), 116, 1135

(3) DeFrees, S.A., et al., J. Am. Chem. Soc., (1995), 117, 66

(4) Ito, Y., et al., Pure Appl. Chem., (1993), 65, 753.

However, when attempting to develop a sugar chain derivative for use as an inhibitor based on an intrinsic sugar chain structure, numerous disadvantages are presented due to the undesirable properties of saccharides.

The primary disadvantage of developing saccharide derivatives for therapeutics resides in the synthesis of these compounds. In spite of the current progress in synthetic methods, numerous difficulties and long steps are still required to synthesize oligosaccharides. Although the techniques used for synthesis of saccharides can be broadly divided into organic chemistry techniques, enzymatic techniques and hybrid forms of the two, each technique, as well as the resulting oligosacchride product, has its own disadvantages.

First, in the case of organic chemistry synthesis techniques, the glycosylation reaction, which serves as the basis of the synthesis, has been exhaustively researched in recent years to the extent that now, it is becoming possible to synthesize any desired sugar chain derivatives. However, since precise synthesis requires identification of numerous other hydroxyl groups which are co-existent, numerous steps including protection, deprotection and selection of those related protecting groups, as well as activation of the saccharide donor are required, thereby making it difficult to realize volume production and synthesis of a large number of sugar chain derivatives. The syntheses of sialyl Lex and gangliosides are examples of this case.

On the other hand, in the case of enzymatic techniques, products can be obtained with high selectivity under mild conditions by utilizing the substrate specificity of glycotransferases and glycohydrolases. However, in addition to problems with ease of acquisition of these enzymes, price and volume production, these techniques also have the disadvantage of lacking the ability for application and development to sugar chains having different structures due, conversely, to the high degree of substrate specificity. The enzymatic synthesis of sialyl Lex is shown as one example of this case.

Second, the oligosacchrides may lack chemical and physiological stability. Since sugar chains are basically

composed of an O-glycoside bond having a hemiacetal structure, they are essentially unstable under acidic conditions. In particular, the O-glycoside bonds of sialic acid and fucose found in sialyl Lex that form the important active site in intercellular interactions and receptor functions, are known to be unstable under acidic conditions. In addition, since these oligosacchrides naturally serve as substrates of numerous glycotransferases and glycohydrolases, it is considered difficult for them to maintain a constant concentration in the blood for a sustained period of time.

Third, the oligosacchrides may not have an appropriate rate of biological absorption. Since the surface of a sugar chain is covered with many hydroxyl groups, they are typically highly hydrophilic, and consequently cannot be expected to be absorbed orally from the gastric mucosa. In addition, they also have a low degree of cell membrane permeability, which results in the undesirable property of lowering their rate of biological absorption.

As a result of these problems with the priocart compounds, several research projects involving sialyl Lex derivatives have been, reported, for instance, in which the pharmacologically active center of the sugar chain structure is replaced with a stable analogue (see Rao, N., et al., J. Biol. Chem., (1994), 269, 19663; Kogan, T.P., et al., J. Med. Chem., (1995), 38, 4976; Uchiyama, T., et al., J. Am. Chem. Soc., (1995), 117, 5395; Kaila, N., et al., Tetrahedron Lett., (1995), 36, 5503; Allanson, N.M., et al., Tetrahedron:Asymmetry, (1994), 5, 2061; and Postema, M.H.D., Tetrahedron, (1992), 48, 8545).

Of those glycoepitopes whose structures and the physical roles have been elucidated, sialyl Lewis X [NeuNAcA2/3Ga/B1-4 (Fucd1/3)GlcNAc is currently of particular interest.

The sialyl LeX, terminal tetrasaccharide glycoepitope of glycolipids and glycoproteins expressed on the cell surface of leukocytes, has been identified as a primary ligand for

selectins (E-, L-, P-) which mediates the initial stage of adhesion of leukocytes to activated endthelial cells in areas of inflammation. Thereafter, leukocytes migrate the sites of inflammation.

Adhesion of leukocytes to the "activated" endothelium is the critical process that initiates the host defense, as well as the progression of the inflammatory response. Intervention in this cell-cell interaction process can therefore provide novel therapeutics for the treatment of pathophysiological conditions arising due to uncontrolled migration of leukocytes under acute and/or chronic conditions. It is now well known that sialyl Lex-type carbohydrates, a number of which are expressed on circulating leukocytes, play a dominant role in their initial attachment to the endothelial cells that line the blood capillaries. This locking-on is mediated through a family of adhesion proteins known as P-, E-and L-selectins. Of these, L(leukocyte)-selectin (LECAM-1, LAM-1) is constitutively present on the surface of the leukocyte. Originally described as MEL-14, it is involved in the trafficking of granulocytes and lymphocytes in the peripheral lymph nodes. (McEver, R.P., Curr. Opin. Immunol. (1994), 6, 75-84; Gallatin, W., et al., Nature (1983), 304, 30-34; Lewinsohn, D.M., et al., J. Inmunol. (1987), 138 4313-4321; Julia, M.A., et al., J. Immunol. (1989) 143, 3318-3324; Watson, S.R., et al., Nature (1991), 349, 164-167; and Kansas, G.S. APIMS (1992), 100, 287-293).

P(platelet)-selectin, also known as granule membrane protein-140 (GMP-140) (Johnston, G.I., et al., Cell (1989), 56, 1033-1044) or platelet activation-dependent granule-external membrane (PADGEM) (Hsu-Lin, S.C., et al., J. Biol. Chem. (1984), 259, 9121-9126) protein, currently designated CD62, is found on activated platelets as well as activated endothelium. It is rapidly exteriorized from the intercellular store (Wiebel-Palade bodies) upon stimulation by thrombin, histamine or phorbol esters (Lasky, L.A., Science (1992), 258, 964-969;

and Hattori, R., et al., J. Biol. Chem. (1989), 264, 9053-9060).

E(endotheiial)-selectin, also known as endothelium leukocyte adhesion molecule-1 (ELAM-1), is transiently expressed only on the surface of the endothelium under the influence of cytokines (Bevilacaua, M.P., et al., Science (1989), 243, 1160-1165).

The three known members of this family contain a domain with homology to the calcium-dependent lectins, an EGF-like domain, and several complement binding protein-like domains (Bevilacqua et al., Science, (1989), 243, 1160-1165; Johnston et al., Cell, (1989), 56, 1033-1044; Lasky et al., Cell, 1989), 56, 1045-1055; Tedder et al., J. Exio. Med., (1989), 170, 123-133; Dasgupta et al., Exp. Opin. Invest Drugs, (1994) 3, 709).

All three selectins recognize a family of sialylated, sulfated and fucosylated carbohydrates (Bevilacqua, M.P., et al., J. Clin. Invest., (1993), 91, 379-387; Brandley, B.K., et al., Cell, (1990) , 63, 861-863; Hakomori, S. I., Histochemical J., (1992), 24, 771-776; Feizi, T., Curr. Opin. Struct. Biol., (1993), 3, 701-710; Green, P.J., et al., Biochem. Bionhys. Res. Comm., (1992), 188, 244-251; and Yuen, C.-T., et al., Biochemistry, (1992), 31, 9126-9131) that are constituents of the glycolipids and glycoproteins found on the leukocyte membrane. The smallest carbohydrate epitopes that have been implicated as ligands for the selectins are siaiyl Lewis x(sLe^x), sulfo Lewis x and sialyl Lewis a (sLe^a) (Tiemeyer M., et al., Proc. Nat'l. Acad. Sci., (1991), 88, 1138-1142; Phillips, M.L., et al., Science, (1990), 250, 1130-1132; Walz, G., et al., Science, (1990), 250, 1132-1135; Foxall C., et al., J. Cell Biol., (1992), 117, 895-902; Handa, K., et al., Biochem. Biophys. Res., (1991), 181, 1223-1230; Polley, M.I., et al., Proc. Natl. Acad. Sci., (1991), 88, 6224-6228; Berg,

E.L., et al., J. Biol. Chem., (1991), 23, 14869-14872; and Zhou, Q., et al., J. Cell Biol., (1991), 115, 557-564).

The key steps leading to the extravasation of the white blood cells are described as follows: P-and E-selectins, expressed on the endothelium under the influence of cytokines, cause "rolling" of the leukocytes by interacting with their cell surface carbohydrates. This initial event is followed by the activation of proteins called integrins on the leukocytes and binding with intercellular adhesion molecules (ICAMs) on the endothelium causing firm adhesion. The leukocytes or the white blood cells can then squeeze out (diapedese) through the endothelium into the adjacent tissues and chemotaxi to the site of the injury. Migration of various subsets of leukocytes such as, neutrophils, macrophages, T-cells etc., is controlled and regulated by specific cytokines (Beekhuizen, H., et al., J. Leukocyte Biol., (1993), 54, 363-378).

A number of reports and reviews have appeared with a description of these events (Adams, D.H., et al., Lancet, (1994), 343, 831-836; Smith, C.W., In: Adhesion: Its Role in Inflammatory Diseases, (1992), Harlan, J.M., et al. (Eds), W.H. Freeman and Co., New York, p83-115; Lawrence, M.B., et al., Cell, (1991), 65, 859-873; Springer, T.A., et al., Nature, (1991), 349, 197; Fukuda, M., et al., J. Biol. Chem., (1986), 261, 12796-12806; Springer, T.A., Nature, (1990), 346, 425-434, Zimmerman, G.A., et al., Immunology Today, (1992), 13 93-99; Stoolman, L.M., Cell Biol., (1989), 907-910; Shimizu, Y., et al., Immunology Today, (1992), 13, 106-111; Osborn, L., Cell, (1990), 62, 3-6; Leewenberg, J.F.M., et al., Scand. J. Immunol., (1992), 35, 335-341; Pober, J.S., et al., Adv. Immunol., (1991), 50, 261-302; and Butcher E.C., 54th Forum in Immunology, (1993), 695-698).

With the understanding that the adhesion process is intrinsically related to all inflammation and that individual events in the inflammation cascade are not isolated, a drug

targeted to this process may have applications for several disease indications.

For instance, Buerke et al. have demonstrated the important role in inflammatory states, such as ischemia-reperfusion injury in cats (Buerke, M. et a., J. Chin. Invest., (1994), 93, 1140). Turunen et al. have demonstrated the role of sLe^x and L-selectin in site-specific lymphocyte extravasation in renal transplants during acute rejection (Turunen, J.P. et al., Eur. J. Immunol., (1994), 24, 1130). P-selectin has been shown to be centrally involved, particularly as related to acute lung injury. Mulligan et al. have reported strong protective effects using anti-P-selectin antibody in a rodent lung injury model (Mulligan, M.S., et al., J. Chin. Invest., (1991), 90, 1600; Mullingan, M.S. et al., Nature, (1993), 364, 149). A central role of P-selectin in inflammation and thrombosis has been demonstrated by Palabrica et al. (Palabrica, T. et al., Nature, (1992), 359, 843).

Of the three selectins, E-selectin is particularly interesting because of its transient expression on endothelial cells in response to IL-1 or TNF (Bevilacqua et al., Science, (1989), 243, 1160). The time course of this induced expression (2-8 hours) suggests a role for this receptor in initial neutrophil extravasation in response to infection and injury. Indeed, Gundel et al. have shown that an antibody to E-selectin blocks the influx of neutrophils in a primate model of asthma and thus is beneficial for preventing airway obstruction resulting from the inflammatory response (Gundel R.H. et al., Chin. Invest., (1991), 88 1407).

Several different groups have published papers regarding E-selectin ligands. Lowe et al., Cell, (1990). 63, 475 demonstrated a positive correlation between E-selectin dependent adhesion of HL-60 cell variants and transfected cell lines, with their expression of the sialyl Lewis x (sLe^x) oligosaccharide, NeuNAc ∀-2-3Gal-∃1-4 (Fuc ∀-1-3) -GlcNAc. By

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transfecting cells with plasmids containing an ∀-(1, 3/1,4) fucosyltransferase, they were able to convent non myeloid COS or CHO lines into sLeX-positive cells that bind in an E-selectin dependent manner. Walz et al., Science, (1990), 250, 1132, were able to inhibit the binding of an E-selectin-IgG chimera to HL60 cells with a monoclonal antibody directed against sLeX or by glycoproteins with the sLeX structure, but could not demonstrate inhibition with CD65 cr CD15 antibodies. Both groups concluded that the sLeX structure is the ligand for E selectin.

On the other hand, inhibitors of the glucosyltransferases which are involved in the biosynthetic process of sialyl Lewis X could be good targets.

Fucosyltransferase is the key enzyme of sLe^x synthesis that transfers fucose to sugar chain as the substrate of GDP-fucose in the final step of sLe^x biosynthesis (Natsuka et al., Cur. Opi. Struc. Biol., 1995, 4 (632-697). There is evidence that this fucosyltransferase is able to be regulated by cell adhesion mediated by selectin (Lowe et al., Cell, (1990), 631, 475-484). Until now, there have been known to exist five isoforms of fucosyltransferase ranging from type III to type VII. Among these five subtypes, type VII has been clearly shown to be involved with the endothelial cells of leukocytes (Sasaki et al., J. Biol. Chem., (1994), 269, 14730-14737). Thus, compounds that possess activity that inhibits this type VII fucosyltransferase would be useful as an anti-inflammatory drug. Although one analogue of GDP-fucose has been reported as an inhibitor of fucosyltransferase (FT), its effects are weak. As such, there are no inhibitors at present that exhibit potent effects while also being specific (Shaopei et al., J. Org. Chem., (1992), 57, 6693-6696).

Using this adhesion-migration paradigm, novel therapeutics can be devised which will intervene with the initial attachment of the leukocytes. This should essentially arrest the

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subsequent events leading to the unwanted proliferation of the leukocytes in the tissues causing damage to the organ. Such compounds will have the potential for treatment of pathological processes such as cardiogenic shock (ischaemia-reperfusion injury), stroke, thrombosis, rheumatism, psoriasis, dermatitis, acute respiratory distress syndrome (ARDS), and even metastasis in which sLe^x and related structures have been implicated (Ogawa, J., et al., Cancer, (1994), 73, 1177-1183; Aruffo, A., et al., Proc. Natl. Acad. Sci. USA, (1992), 89, 2292-2296; Kojima, N., et al., Biochem. Bioohys. Res. Commun., (1992), 182, 1288-1295; Takada, A., et al., Cancer Res., (1993), 53, 354-361; and DeJana, E., et al., Laboratory Investigation, (1992), 66, 324-330).

Summary of the Invention

The present invention relates to aryl C-glycoside compounds comprising an aryl part and a glycosyl part, wherein the aryl part represents a phenyl acetic acid moiety which provides an anti-inflammation effect, which is unsubstituted or can be substituted with more than one 1'-lycosyl compound and the glycosyl part represents a natural or artificial monosaccharide having an α or β bond, or a disaccharide, a trisaccharide or a tetrasaccharide of said monosaccharide, the saccharides being unsubstituted or substituted by at least with a carboxyalkyl group or an acyl group; or a sulfate ester thereof or a pharmaceutically acceptable salt thereof. Particularly preferred compounds are described throughout the specification.

The present invention is further directed to a method for treating or preventing an inflammatory disease, an auto-immune disease, an infection, cancer, a reperfusion disorder, thrombosis, ulcer, a wound or osteoporosis in a mammal, such as a human, comprising administering to mammal (such as a human) a pharmaceutically effective amount of the aryl C-glycosides

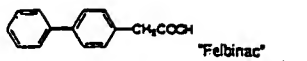
described herein, either alone, or in admixture with a pharmaceutically acceptable excipient.

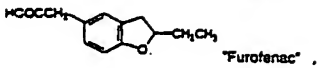
Finally, the present invention also concerns processes for the preparation of the invention compounds.

Detailed Description Of The Invention

As a result of research by the inventors of the present invention for the purpose of obtaining a chemically and physiologically stable glycomimic that mimics the important role played by sugar chains in the body, but eliminates those undesirable properties inherently possessed by sugar chains, it was discovered that aryl C-glycoside compounds and their sulfated forms have various pharmacological activities related to sugar chains.

In the C-glycoside compounds of the present invention having an aryl part and a glycosyl part, the aryl part is a phenyl acetic acid moiety which provides an anti-inflammatory effect, examples of which include the following:


"Felbinac"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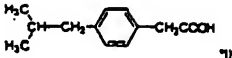
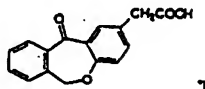

"Ibufenac"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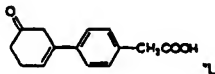
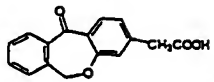
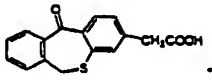
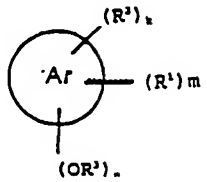

"Lexofenac"


"Oxepinac"


"Tiopinac"



(I)

The present invention also concerns an aryl C-glycoside of the formula (I)

The glycosyl part of the compounds of the present invention and R^1 of the compounds of formula (I) are a natural monosaaccharide having an α or ß bond, which may be a D-form or a L-form, preferably a natural form of the sugar. Examples of such groups include glucose, glucosamine, galactose, gaiactosamine, fucose, mannose, sialic acid, ribose, rhamnose,

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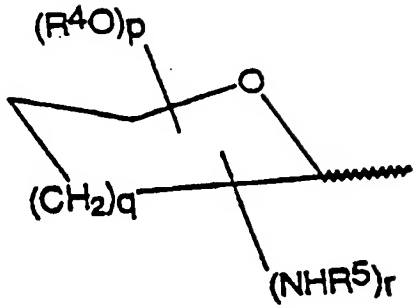
xylose, arabinose, lyxose, 2-deoxygalactose, 2-deoxyglucose, fructose, sorbose, allose, aitrose, talose, tagatose, glucronic acid and galacturonic acid, of which galactose, fucose and xylose are preferred.

R^1 can also be an artificial monosaccharide having an α or ß bond, which may be a D-form or a L-form. Examples of such groups include a pyranose and furanose, which has an oxygen atom in a ring, in which a hydroxy group is attached to the carbon atom next to the ring oxygen atom and some hydroxy groups may be substituted.

For example, the monosaccharide of R^1 for the compounds of formula



(II)

(I) set forth above can have the formula (II):

wherein R^4 represents a hydrogen atom, a carboxyalkyl group or an acyl group;

R^5 represents a hydrogen atom or an acyl group;

p represents an integer of 1 to 5;

q represents an integer of 1 or 2; and

r represents 0 or 1.

Where R^1 represents a disaccharide having an α or β bond, this may be a D-form or a L-form, preferably a natural form of the sugar. Examples of such groups include natural

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disaccharides such as lactose, maltose, cellobiose, gentiobiose and melibiose and artificial disaccharides comprising à dimer of sugar-like compounds (an oxygen atom is contained in a ring, a hydroxy group is attached to the carbon atom next to the ring oxygen atom and some hydroxy groups may be substituted), of which natural disaccharides are preferred.

Where R^1 in the compounds of formula (1) represents a trisaccharide having an α or β bond, this may be a D-form or a L-form, preferably a natural form of the sugar. Examples of such groups include natural trisaccharides, such as maltotriose and artificial trisacchardies comprising a trimer of sugar-like compounds, of which natural trisaccharides are preferred.

Where R^1 of the compounds of formula (I) represents a tetrasaccharide having an α or β bond, this may be a D-form or a L-form, preferably a natural form of the sugar. Examples of such groups include natural tetrasaccharides such as maltotetraose and artificial tetrasaccharides comprising a tetramer of sugar-like compounds, of which natural trisaccharides are preferred.

Where (Ar), of the compounds of formula (I) represents an aromatic compound, this may be a mono aryl compound, a biaryl compound or a triaryl compound, containing from 6 to 18 carbon atoms, preferably from 6 to 12 carbon atoms. Examples of such groups include an aryl compound such as benzene, naphthalene, anthracene, phenanthrene, indene, fluorene, stilbene, indan, 1, 2, 3, 4-tetrahydronaphthalene, 9, 10-dihydroanthracene, 9, 10-dihydrophenanthrene, aromatic steroids, e.g., estradiol; a biaryl compound; such as biphenyl, diphenylmethane, diphenylethane, diphianyl ether; or a triaryl compound, of which benzene and naphthalene are preferred.

Where (Ar) of the compounds of formula (I) also represents an heterocyclic aromatic compound, this may be a 5 to

14-membered heteroaryl compound, which may optionally be condensed. The ring members of which heterocyclic aromatic compound include 1 to 3 sulfur, oxygen and/or nitrogen atoms. (Ar) may also be a bi-heteroaryl compound or a tri-heteroaryl compound, containing from 6 to 18 carbon atoms, preferably from 6 to 12 carbon atoms. Examples of such compounds include xanthene, furan, benzofuran, dibenzofuran, chromanone, flavone, flavanone, thiophene, thianaphthene, pyrrole, pyrazole, imidazole, oxazole, isoxazole, isothiazole, thiazole, 1, 2, 3-oxadiazole, triazole, tetrazole, thiadiazole, pyridine, pyridazine, pyrimidine, purazine, indole, indazole, purine, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbozole, carboline, phenanthridine or acridine; of which is preferred an aromatic, 5-to 10-membered, heterocyclic group which may optionally be condensed, among the ring members of which 1 to 2 sulfur and/or oxygen atoms are included. More preferably, as represents furan, benzofuran, dlibenzofuran, chromanone, flavone, flavanone, thianaphthene or thiophene.

R^2 of the compounds of formula (I) also represents a halogen atom, which may be a fluorine atom, a chlorine atom, a bromine atom, or an iodine atom; of which is preferred a flourine atom and a chlorine atom.

R^2 of the compounds of formula (I) also represents a straight, branched or cyclic alkyl group, containing from 1 to 10 carbon atoms, preferably from 1 to 8 carbon atoms. Examples of such groups include a straight or branched alkyl group such as methyl, ethyl, propyl, 1-methylethyl, butyl, 1-methylpropyl, 2-methylpropyl, 1,1-dimethylethyl, pentyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 1,1-dimethylpropyl, 2,2dimethylpropyl, 1,2-dimethylpropyl, 1-ethylpropyl, hexyl, 1-methylpentyl, 2-methylpentyl, 1,1-dimethylbutyl, 1,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1-methyl-

lethylpropyl, heptyl, 1-methyl-1-ethylbutyl, 2-methyl-2-ethylbutyl, octyl, 1-methylheptyl, 2-ethylhexyl, 1,1,3,3-tetramethylbutyl, nonyl, decyl or 3,7-dimethyloctyl, of which is preferred a straight or branched alkyl group containing from 1 to 3 carbon atoms, more preferably a methyl group and an ethyl group; a cyclic alkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl and perhydronaphthalene, of which is preferred a cyclic alkyl group containing from 3 to 6 carbon atoms, more preferably cyclopentyl and cyclohexyl; or a cycloalkyl-alkyl group such as cyclohexylmethyl and cyclohexylethyl.

When R^2 of the compounds of formula (I) represents a straight, branched or cyclic alkyl group, this group can be cyclized with the (Ar) group to a condensed ring group.

Where an aryl C-glycoside of the formula (I) represents a salt thereof, this may be a metal salt of a carboxy group, a carboxyalkyl group or a sulfonic acid group. Examples of such metal salts include salts of alkali metals such as sodium, potassium or lithium; alkaline earth metals such as barium or calcium; and another metal such as magnesium, aluminum, iron, zinc, copper, nickel or cobalt, of which is preferred an alkali metal.

Where R^3 of the compounds of formula (I) represents an alkyl such alkyl group is as defined above for R^2.

Where R^1, R^3, R^4 or R^5 of the compounds of formula (I) rerpresents an acyl group, this may be a straight or branched acyl group containing from 1 to 10 carbon atoms, preferably from 1 to 3 carbon atoms, more preferably an acetyl group. Examples of such groups include aliphatic acyl groups, preferably acyl groups having from 1 to 25 carbon atoms, more preferably from 1 to 20 carbon atoms, still more preferably from 1 to 6 carbon atoms, and most preferably from 1 to 4 carbon atoms, such as the formyl, acetyl, propionyl, butyryl,

isobutyryl, pivaloyl, valeryl, isovaleryl, hexanoyl, heptanoyl, octanoyl, lauroyl, myristoyl, tridecanoyl, palmitoyl and stearoyl groups, of which the acetyl group is most preferred; halogenated alkanoyl groups having from 2 to 6 carbon atoms, preferably halogenated acetyl groups, such as the chloroacetyl, dichloroacetyl, trichloroacetyl and trifluoroacetyl groups; lower alkoxyacyl groups in which the alkoxy part has from 1 to 6, preferably from 1 to 3, carbon atoms and the acyl part has 2 to 6 carbon atoms and is preferably an acetyl group, such as the methoxyacetyl group; and unsaturated analogs of such groups, especially alkenoyl or alkynoyl groups having from 3 to 6 carbon atoms, such as the acryloyl, methacryloyl, propioloyl, crotonoyl, isocrotonoyl and (E)-2-methyl-2-butenoyl groups; aromatic acyl groups, preferably arylcarbonyl groups, in which the aryl part from 6 to 14, more preferably 6 to 10 and most preferably 6, ring carbon atoms, and is a carbocyclic group, which is unsubstituted or has from 1 to 5, preferably from 1 to 3, substituents, selected from the group consisting of substituents A (defined hereinbelow), for example, unsubstituted groups, such as the benzoyl, (α-naphthoyl and β-naphthoyl groups; halogenated arylcarbonyl groups, such as 2-bromobenzoyl and 4-chlorobenzoyl groups; lower alkyl-substituted arylcarbonyl groups, in which each alkyl substituent has from 1 to 6, preferably from 1 to 4, carbon atoms, such as the 2,4,6-trimethylbenzoyl and 4-toluoyl groups; lower alkoxy-substituted arylcarbonyl groups, in which the or each alkoxy substituent preferably has from 1 to 6, more preferably from 1 to 4, carbon atoms, such as an 4-anisoyl group; carboxy-substituted arylcarbonyl groups, such as 2-carboxybenzoyl, 3-carboxybenzoyl and 4-carboxybenzoyl groups; nitro-substituted arylcarbonyl groups, such as 4-nitrobenzoyl and 2-nitrobenzoyl groups; lower alkoxycarbonyl-substituted arylcarbonyl groups, in which each alkoxycarbonyl substituent

preferably has from 2 to 6 carbon atoms, such as an 2-(methoxycarbonyl)benzoyl group; and aryl-substituted arylcarbonyl groups, in which the aryl substituent is as defined above, except that, if it is substituted by a further aryl group, that aryl group is not itself substituted by an aryl group, such as the 4-phenylbenzoyl group; alkoxycarbonyl groups, especially such groups having from 2 to 7, more preferably 2 to 5, carbon atoms and which may be unsubstituted, such as methoxycarbonyl, ethoxycarbonyl, t-butoxycarbonyl and isobutoxycarbonyl groups or substituted with a halogen atom or a tri-substituted silyl group, e.g., a tri(lower alkylsilyl) group, such as the 2,2,2-trichloroethoxycarbonyl and 2-trimethylsilylethoxycarbonyl groups; alkenyloxycarbonyl-groups in which the alkenyl part has from 2 to 6, preferably from 2 to 4, carbon atoms, such as the vinyloxycarbonyl and allyloxycarbonyl groups; and aralkyloxycarbonyl groups, in which the aryl ring, if substituted, is substituted by at least one substituent selected from the group consisting of substituents A (defined hereinbelow), one or two lower alkoxy or nitro substituents, such as benzyloxycarbonyl, 4-methoxybenzyloxy-carbonyl, 3, 4-dimethoxybenzyloxycarbonyl, 2-nitrobenzyloxycarbonyl and 4-nitrobenzyloxycarbonyl groups.

The substituents A include halogen atoms such as fluorine, chlorine, bromine and iodine; an alkyl group such as defined above for R'; an alkoxy group having 1 to 10 carbon atoms and preferably 1 to 6 carbon atoms; a carboxy group, a nitro group; an alkoxycarbonyl group with the alkoxy group thereof having 1 to 10 carbon atoms and preferably 1 to 6 carbon atoms; and an aryl group as defined above.

Where R^1 or R^4 represents a carboxyalkyl group, the alkyl part thereof is as defined above in the definition of R^2.

The compounds of the present invention may contain one or more asymmetric carbon atoms in their molecules, and, in such a case, can thus form optical isomers.

Although the compounds are all represented herein by a single molecular formula, the present invention includes both the individual, isolated isomers and mixtures, including racemates thereof. Where stereospecific synthesis techniques are employed or optically active compounds are employed as starting materials, individual isomers may be prepared directly. On the other hand, if a mixture of isomers is prepared, the individual isomers may be obtained by conventional resolution techniques.

Preferred classes of compounds of the present invention are those compounds of formula (I) and pharmaceutically acceptable salts and sulfate esters thereof in which:

(1) R^1 represents a natural or artificial monosaccharide having an (α or β bond, wherein the saccharide is unsubstituted or is substituted with carboxyalkyl groups or acyl groups;

(2) R^1 represents a natural monosaccharide having an (α or β bond;

(3) m represents an integer of 1 to 2;

(4) m represents 1;

(5) (Ar), represents an aromatic group;

(6) R^2 represents a straight, branched or cyclic alkyl group which is unsubstituted or is substituted with an oxo group, a hydroxy group, a carboxy group or a sulfonic acid group, and R^2 represents a straight, branched or cyclic alkyl group, this group can be cyclized with the (Ar) group to a condensed ring group;

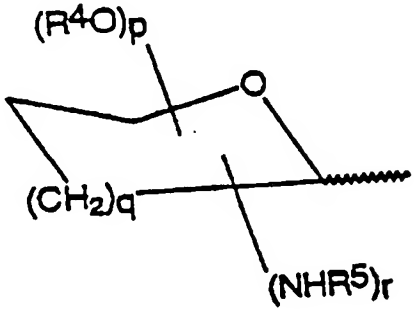
(7) R^2 represents a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, and this group can be cyclized with the (Ar) group to a condensed ring group;

(8) R^2 represents a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group;

(9) R^2 represents a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a suifonic acid group;

(10) k represents an integer of 1 to 2); when k does not represent 1, the R^2 groups are the same or different;

(11) R^3 represents a hydrogen atom or an alkyl group;



(II)

(12) n represents an integer of 1 to 2;

(13) R^1 represents the following formula (II):

wherein,

R^4 represents a hydrogen atom;

R^5 represents a hydrogen atom;

p represents an integer of 1 to 5;

q represents an integer of 1 or 2; and

r represents zero.

As discussed hereinabove, important compounds of the present invention include the following:

[2-(ß-L-fucopyranosyl)-3,4,5-trimethoxyphenyl] acetic acid,

[3-(ß-L-fucopyranosyl)-4-methoxyphenyl]acetic acid,

1-(3-(ß-L-fucopyranosyl)-4-methoxyphenyl] cyclohexanecarboxylic acid,

[3-(ß-L-fucopyranosyl)-4-methoxyphenyl]butyric acid,

1-(3-ß-D-galactopyranosyl)-4-methoxyphenyl] cyclohexanecarboxylic acid,

1-[4-methoxy-3-(ß-L-rhamnopyranosyl)phenyl] cyclohexanecarboxylic acid,

1-[4-methoxy-3-(ß-D-xylopyranosyl)phenyl] cyclohexanecarboxylic acid,

6-(ß-L-fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) benzene,

1-(ß-L-fucopyranosyl)-2, 6-dimethoxy-5 (5-acetamido-3, 5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) naphthalene, and

2,6-dimethoxy-1-(sodium ß-D-galactopyranosyl 2,3,4, 6-tetrasulfate)-5-(sodium ß-L-fucopyranosyl 2,3,4-trisulfate) naphthalene.

Aryl C-glycoside compounds are not susceptible to hydrolysis under acidic conditions and glycohydrolases as a result of the anomeric carbon of the saccharide being directly connected with an aromatic compound by carbon-carbon bonds. In addition, since aryl C-glycoside compounds are resistant to modification without being the inherent substrate of glycotransferases, aryl C-glycoside compounds are considered to be stable and active for a sustained period of time in the body. Moreover since aryl C-glycoside compounds possess both the hydrophilicity of saccharides and the lipophilicity of aromatic compounds, aryl C-glycoside compounds are expected to

exhibit suitable solubility in aqueous systems of the compound, as well as permeability with respect to the cell membrane.

The following publications concern C-glycosylation:

(1) Jaramillo, C.; Knapp, S., Synthesis, (1994), 1-20

(2) Postema, M.H.D., Tetrahedron, (1992), 48, 8545-8599

(3) Postema, M.H.D., C-Glycoside Synthesis, CRC Press, (1995), 265-301.

The following publications report other work in this field:

(1) Matsumoto, T.; et al., Tet. Lett., (1988), 29,6935

(2) Matsumoto, T.; et al., Tet. Lett., (1989), 30, 833

(3) Matsumoto, T.; et al., Tet. Lett., (1989), 30, 6185

(4) Matsumoto, T.; et al., Tet. Lett., (1990), 31, 4629

(5) Toshima, K.; et al., Tet. Lett., (1992), 33, 2175

(6) Toshima, K.; et al., J. Chem. Soc., Chem. Commun., (1992), 1641

(7) Ohrui, H.; et al., Agr. Biol. Chem., (1972) , 36, 1651

(8) Mahling, J.A. et al., Synthesis, (1993), 325

(9) Stewart, A.O.; et al., J. Am. Chem. Soc., (1985), 107, 4289.

(10) Williams, R.M.; et al., Tet. Lett., (1983), 24, 2715

(11) Outten, R.A.; et al., J. Org. Chem., (1991), 56, 5064

(12) Kwok, D.I.; et al., J. Org. Chem., (1991.), 56, 37

(13) Dubois, E.; et al., J. Chem. Soc., Chem. Commun., 1990), 1191.

The following publications are directed to the synthesis of natural aryl C-glycosides:

(1) Matsumoto, T.; et al., J. Am. Chem. Soc., (1991), 113, 6982

(2) Matsumoto, T.; et al., J. Am. Chem. Soc., (1992), 114, 3568

(3) Hosoya, T.; et al., J. Am. Chem. Soc., (1994), 116, 1004.

One advantage of the present method for the synthesis of aryl C-glycoside compounds is that numerous saccharides constituting the primary sugar chain in the living body, including glucose, glucosamine, galactose, galactosamine, fucose, mannose, sialic acid, ribose, rhamnose and xylose, can serve as the donor substrate.

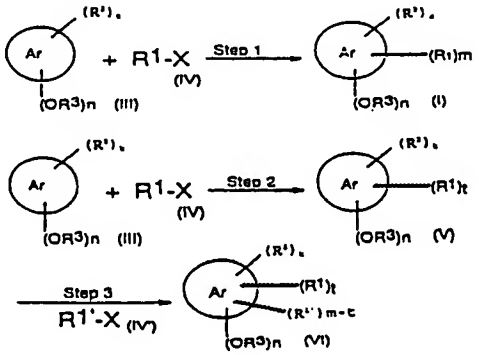
Another advantage of the present method is that easily obtainable and stable 1-lower alkanoyl, 1-benzoyl, 1-lower alkyl and 1-hydroxy derivatives can be used as the donor without the need for special elimination groups. Stated differently, heretofore derivatives of sugars such as sugar halide, sugar imidate or thioglycoside (sugar as such cannot be reacted directly), which is usually unstable and has a strange odor, were required to glycosylate a material to convert a sugar to a relevant derivative. However, in the present process, a sugar per se can be used which is stable and easily obtainable, as a sugar donor. This is an important advantage. Thus, in the present invention, since aromatic compounds not having a relatively high electron density can be used as the aromatic compound that serves as the saccharide receptor, various types of derivatives can be synthesized in a small number of steps. The diversity and universality of this technique is shown in the Examples set forth hereinbelow.

The efficacy of the pharmacological effects of these compounds is discussed herein in terms of their cell adhesion molecular inhibition effect. Fucosyltransferase (FT) VII inhibitory effect (FT VII means α (1, 3) fucosyltransferase which catalyses the synthesis of Sialyl Lewis X and expresses selectin ligands (see pages 686-687 of S. Natsuka et al., Current Ovinion in Stuctural Biology, 4, 683-691, (1994)). The latent properties of these compounds are not limited to the above-mentioned activities, but are expeted to demonstrate pharmacological effects related to a broad range of biological

activities involving sugar chains in the form of chemically and physiologically stable glycomimics.

Synthesis:

The subject compounds can, be synthesized in accordance with the following method:



A detailed description of the reagents and reaction conditions used in the aryl C-glycosidation reaction is set forth in the Examples hereinbelow.

In the above formulae R^1, R^2, R^3, (Ar), k, m and n are as defined above.

X represents a leaving group, where there is no particular limitation upon the nature of the leaving group, provided that it is a group capable of leaving as a nucleophilic residue, such as are well known in the art. Examples of preferred leaving groups include the following: hydroxy groups; halogen atoms, such as fluorine, chlorine, bromine and idodine atoms; alkylcarbonyloxy groups, such as acetoxy, ethylcarbonyloxy, propylcarbonyloxy and butylcarbonyloxy groups; aralkylcarbonyloxy groups, such as benzoyl, benzylcarbonyloxy and phenethylcarbonyloxy groups; lower alkoxycarbonyloxy groups, such as methoxycarbonyloxy and ethoxycarbonyloxy

groups; halogenated alkylcarbonyloxy groups, such as chloroacetoxy, dichloroacetoxy, trichicroacetoxy and trifluoroacetoxy groups; lower alkanesulfonyloxy groups, such as methanesulfonyloxy and ethanesuifonyloxy groups; lower haloalkanesulfonyloxy groups, such as trifluoromethanesulfonyloxy and pentafluoroethanesulfonyloxy groups; and arylsulfonyloxy groups, such as benzenesulfonyloxy, p-toluenesulfonyloxy and p-nitrobenzenesulfonyloxy groups. Of these, alkylcarbonyloxy groups, aralkylcarbonyloxy groups, hydroxy groups, halogen atoms, lower haloalkanesulfonyloxy groups and arylsulfonyloxy groups are preferred and alkylcarbonyloxy groups and aralkylcarbonyloxy groups are most preferred;

t represents an integer of 1 to 2.

$R^{1'}$ represents a different group from R^1 and is as defined above with respect of R^1.

In Steps 1 and 2, the compound of the formula (I) or the formula (V) is prepared by a condensation reaction of compounds of the formulae (III) and (IV) in the presence of a mixed catalyst containing a Lewis acid and solvent.

There is no particular limitation on the mixed catalyst containing a Lewis acid. Any Lewis acid catalyst commonly used in a condensation reaction of this type may be employed. Examples of such catalysts include metal halides such as stannous tetrachloride and gallium chloride and a metal salt of a strong acid such as a silver or mercury salt of trifluoromethanesulfonic acid or trifluoroacetic acid.

The reaction is normally and preferably carried out in the presence of a solvent, the nature of which is not critical, provided that it has no adverse effect upon the reaction and that the solvent can dissolve the reagents, at least to some extent. Examples of suitable solvents include the following: aliphatic hydrocarbons, such as hexane and heptane; aromatic hydrocarbons, such as benzene, toluene and xylene; halogenated

hydrocarbons, such as methylene chloride, chloroform, carbon tetrachloride, dichloroethane, chlorobenzene and dichlorobenzene; esters, such as ethyl formate, ethyl acetate, propyl acetate, butyl acetate and diethyl carbonate; ethers, such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethylene glycol dimethyl ether; nitrites, such as acetonitrile and isobutyronitrile; and amides, such as formamide, dimethylformamide, dimethylacetamide, N-methyl-2-pyrrolidone, N-methylpyrrolidinone and hexamethylphosphoric triamide.

There is no particular limitation on the molar ratio of the compound represented by R^1 and the compound represented by (Ar) and any ratio commonly used in this type reaction may equally be employed. An example of such ratio is 8 : 1 to 1 : 5 (the compound represented by R^1: the compound represented by (Ar)).

The number of sugar moieties which are to be introduced, that is "m" and "t", can vary according to the molar ratio of the compound represented by R^1 and the compound represented by (Ar).

When only one sugar moiety can be introduced at one time, a further sugar moiety may be introduced by repeating the above condensation reaction, if desired.

The reaction can be performed over a wide range of temperatures, and the precise reaction temperature chosed is not critical to the invention. In general, it is convenient to carry out the reaction at a temperature of from -80°C to 100°C, more preferably from 0°C to 300°C. The time required for the reaction may likewise vary widely, depending on many factors, notably the reaction temperature, the starting materials, the solvent employed and the nature of the reagents. However, in most cases, a period of from 30 minutes to 7 days, more

preferably from 3 hours to 2 days, will normally suffice for the reaction.

After completion of this reaction, the desired compound of formula (I) can be collected from the reaction mixture by conventional means. For example, one suitable recovery procedure comprises, if appropriate, neutralizing the pH; if there is a precipitate, removing the precipitate by filtration; adding water to the residue; and extracting the mixture with a water-immiscible organic solvent, such as ethyl acetate. The extract is then dried over anhydrous magnesium sulfate, after which the solvent is removed by distillation, to give the desired compound. If necessary, the resulting compounds can be further purified by conventional means, such as recrystallization or the various chromatography techniques, notably column chromatography.

The condensation product obtained by this reaction can be converted into the compound of the present invention by performing reactions such as hydrolysis, reduction, amidation, and so forth, that are commonly known to those skilled in the art.

In addition, conversion to the sulfated form is normally performed by reacting at 0°C to 100°C for 30 minutes to 1 day using a triethylamine or pyridine complex of sulfur trioxide in a solvent such as dimethylformamide or pyridine.

Concerning the above step 1 for the subject compound, see the following publications:

1) Guilbert, B., et al., Tetrahedron Lett., (1994), 35, 6563
2) Guilbert, B., et al., Tetrahedron Asymmetry, (1994), 5, 2163
3) Lubineau, A., et al., J. Chem. Soc. Chem. Commun., (1993), 1419
4) Lubineau, A., et al., Tetrahedron Lett., (1994), 35, 8795

5) Jain, R.K., et al., J. Am. Chem. Soc., (1994), 116, 12123

6) Bertozzi, C.R., et al., Biochem., (1995), 34, 14271.

In Step 3, the compound of formula (VI) is prepared by a further condensation reaction of compounds (V), as obtained in Step 2, with another sugar moiety represented by (IV') in the presence of a mixed catalyst containing a Lewis acid and a solvent, according to the method as described above for Steps 1 and 2.

The compounds represented by (Ar) are commercially available products or derivatives that can be easily derived from commercially available products using well known conventional means such as esterification, alkylation, reduction, hydrolysis, and so forth, by those skilled in the art.

Some of the compounds, for example, can be synthesized according to the methods as described in Kogan et al., J. Med. Chem., 38, 4976 (1995) and Suzuki et al., Synth. Commun., 11, 513 (1981).

The biphenyl compound can be synthesized by condensation of an aryl halide and an aryl boronic acid in the presence of a palladium catalyst in accordance with the method of the following publications:

1) Miyaura, N., et al., Synth. Commun., (1981), 11, 513

2) Kogan, T.P., et al., J. Med. Chem., (1995), 38, 4976

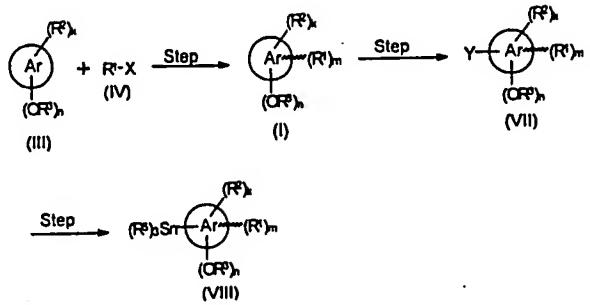
3) Rocca, P., et al., Tetrahedron Lett., (1994), 35, 2003

4) Alo, B.I., et al., J. Org. Chem., (1991), 56, 3763.

The introduction of a plurality of saccharide units serves to expand the diversity of the structure and function of the aryl C-glycoside compound as a glycomimic.

The subject compounds can be also synthesized via glycosylated aryl tin compounds, as described below.

Process A



In the above formula, R^1 , R^2, R^3, (Ar), k, m and n have the same meanings as defined above.

R^6 represents a lower alkyl group or phenyl group.

Y represents a fluorine atom, a chlorine atom, a bromine atom or an iodine atom.

In general, X is not particularly limited as long as it is a group which can be eliminated as a nucleophilic residue. Preferably, X may be a hydroxyl group; a halogen atom such as chlorine, bromine and iodine; an alkylcarbonyloxy group such as acetoxy, ethylcarbonyloxy, propylcarbonyloxy and butylcarbonyloxy; an aralkyloxycarbonyl group such as benzoyl, benzylcarbonyloxy and phenethylcarbonyloxy; a lower alkoxycarbonyloxy group such as methoxycarbonyloxy and ethoxycarbonyloxy; a halogenated alkylcarbonyloxy group such as chloroacetoxy, dichloroacetoxy, trichloroacetoxy and

trifluoroacetoxy; a lower alkanesulfonyloxy group such as methanesulfonyloxy and ethanesulfonyloxy; a halogeno-lower alkanesulfonyloxy group such as trifluoromethanesulfonyloxy and pentafluoroethanesulfonyloxy; an arylsulfonyloxy group such as benzenesulfonyloxy, p-toluenesulfonyloxy and p-nitrobenzenesulfonyloxy; and a leaving group containing a phosphorus atom such as a diphenylphosphate group, P,P-diphenyl-N-tosylphosphine imidate group, N,N,N',N'-tetramethylphosphoroamidate group, phosphorodiamidimidethioate group and diethylphosphite. More preferably, X represents an alkylcarbonyloxy group, an aralkylcarbonyloxy group, a hydroxyl group, a halogen atom, a halogenolower aikanesulfonyl group or an arylsulfonyloxy group. Most preferably, X represents an alkylcarbonyloxy group or an aralkylcarbonyloxy group.

Step A1

Step A1 is a step of preparing an aryl C-glycosyl compound (I) by a condensation reaction of a sugar derivative (III) with an aryl compound (IV) in the presence of a mixed catalyst containing Lewis acid.

The Lewis acid catalyst is not particularly limited so long as it is used in a common condensation reaction. Preferably, the Lewis acid is a metal halide such as stannous tetrachloride, gallium trichloride, zinc bromide and titanium tetrachloride; a metal salt of a strong acid, such as a silver or mercury salt of trifluoromethanesulfonic acid or trifluoroacetic acid; and perchloric acids such as trimethylsilyl perchlorate and triphenylmethyl perchlorate.

The reaction is carried out generally in the presence of a solvent. The solvent to be used is not particularly limited so long as it does not inhibit the reaction and dissolves a starting substance to a certain extent, preferably the solvent is selected from the group of aliphatic hydrocarbons such as

hexane and heptane; aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, dichloroethane, chlorobenzene and dichlorobenzene; esters such as ethyl formate, ethyl acetate, propyl acetate, butyl acetate and diethyl carbonate; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethylene glycol dimethyl ether; nitriles such as acetonitrile, propionitrile and isobutyronitrile; and amides such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl-2 pyrrolidone, N-methylpyrrolidinone and hexamethylphosphorotriamide.

The reaction temperature is not particularly limited, and the reaction is carried out generally at -80°C to 100° C (preferably 0°C to 30°C).

The reaction time varies depending on the kinds of a starting material, a reagent and a solvent and the reaction temperature, and the reaction is completed generally in 30 minutes (preferably 3 hours) to 7 days (preferably 2 days).

The ratio of the sugar derivative (VI) to the aryl compound (III) in this reaction is not particularly limited, the reaction can be carried out generally at 8:1 to 1:5 [Compound (III):Compound (IV)], and the number (i.e., "n") of the sugar residues represented by R^1 to be introduced into the aryl C-glycosyl compound (I) varies depending on the molar ratio of the two starting materials in this reaction. Further, when one sugar residue is introduced in one reaction, if desired, a plurality of the sugar residues can be introduced by repeating the above reaction.

Further, this step can be also carried out by using the reagent for an aryl C-glycosylation reaction disclosed in WO 97/11066.

Step A2

Step A2 is a step of preparing a compound having the formula (VII) by halogenating the aryl C-glycosyl compound (I) according to a known method, and is carried out by, for example, reacting the aryl C-glycosyl compound (I) with a halogenating agent in a solvent in the presence or absence of a catalyst.

The halogenating agent to be used is not particularly limited so long as it is used as a halogenating agent in a common reaction, and there may be mentioned, for example, a fluorinating agent such as fluorine (F2), fluoroxytrifluoromethane, xenon difluoride, cesium acetyl hypofluorite, N-fluorosulfonamide, L diethylaminosulfa trifluoride(DAST) and a N-fluoropyridinium salt (e.g., N-fluoropyridinium, N-fluoro-2,6-di(methoxycarbonyl) pyridinium, N-fluoro-3,5-dichloropyridinium, N-fluoro-2,4,6-trimethylpyridinium N-Fluoro-3, 5-dichloropyridinium, N-Fluoro-2,4,6-trimethypyridinium and the like); a chlorinating agent such as chlorine (C12), N-chlorosuccinimide, cupric chloride, sulfuryl chloride, titanium tetrachloride, 2,3,4,5,6-hexachloro-2,4-cyclohexadienone, 2,3,4,4,5,6,6-hexachloro-2,5-cyclohexadienone, N-chlorotriethylammonium, chloride and benzeneselenenyl chloride; a brominating agent such as bromine (Br_2), bromine chloride, cupric bromide, silver sulfate-bromine, tetramethylammonium tribromide, trifluoroacetyl hypobromide, dibromoisocyanuric acid (DBI), 2,4,4,6-tetrabromocyclohexa-2,5-dienone, hydrogen bromide-dimethyl sulfoxide, N-bromosuccinimide-dimethyl-formamide and 2,4-diamino-1,3-thiazole hydrotribromide; and an iodinating agent such as iodine (I2), iodine monochloride (ICl), 1,3-diiodo-5,5-dimethylhydantoin, an iodine-morpholine complex, trifluoroacetyl hypoiodide, iodine-periodic acid, iodine-thalium (I) acetate, fluorine-iodine and ethyleneiodochloride.

The solvent to be used is not particularly limited so long as it does not inhibit the reaction, and there may be preferably mentioned aliphatic hydrocarbons such as hexane and heptane; aromatic hydrocarbons such as benzene, toluene and xylene; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride, chlorotrifluoromethane, dichloroethane, chlorobenzene and dichlorobenzene; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dioxane, dimethoxyethane and diethylene glycol dimethyl ether; nitriles such as acetonitrile, propionitrile and isobutyronitrile; amides such as formamide, N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl-2-pyrrolidone, N-methylpyrrolidinone and hexamethylphosphorotriamide; lower aliphatic acids such as formic acid, acetic acid and propionic acid; sulfoxides such as dimethyl sulfoxide, and a mixed solvent of them.

As the catalyst to be used, there may be mentioned, for example, a metal halide such as aluminum chloride and ferric bromide; mercuries such as mercury acetate; and metals such as iron.

The reaction temperature is not particularly limited, and the reaction is carried out generally at -120°C (preferably -10°C) to 100°C.

The reaction time varies depending on the kinds of a starting material, a reagent and a solvent and the reaction temperature, and the reaction is completed generally in 2 minutes (preferably 1 hour) to 2 days.

Step A3

Step A3 is a step of preparing a glycosylated aryl tin compound (VIII) by introducing a tin atom into the compound having the formula (VII) in a solvent in the presence of a palladium catalyst and a base according to a known method. For

example, the methods described in the following references may be used:

H. Azizian, et al., J. Organomet. Chem., 215, 49 (1981),
A.N. Kashin, et al., J. Org. Chem. USSR, 17, 789 (1984),
T. Depaulis, et al., Synthetic Commun., 21, 1091 (1991).

The solvent is not particularly limited so long as it does not inhibit the reaction and dissolves a starting substance to a certain extent, and the solvents described in Step A1 may be used.

The palladium catalyst to be used is not particularly limited so long as it is a catalyst containing palladium. Preferably, one of the following palladium catalysts are used: tetrakis(trifluorophosphine)palladium (0), bis[1,2-bis(diphenylphosphino) ethane]palladium (0), bis[o-phenylenebis(diethylphosphine)]palladium (0), bis(cycloocta-1,5-diene) palladium (0), palladium carbon, palladium black, palladium (II) acetate, palladium (II) acetoacetate, palladium (II) chloride, palladium (II) cyanide, palladium (II) trifluoroacetate, [1,2-bis(diphenylphosphino)ethane]dichloropalladium (II), bis(acetonitrile)dichloropalladium (II), bis(acetate)bis(triphenylphosphine) palladium (II), bis(benzonitrile)dichloropalladium (II), [1,1'-bis-(diphenylphosphino)ferrocene]dichloropalladium (II), (2,2'-bipyridine) dichloropalladium (II), (bicyclo[2,2,1]hepta-2,5-diene) dichloropalladium (II), dichloro(1,5-cyclooctadiene] palladium (II), dichlorobis(triphenylphosphine)palladium (II) and the like.

The base to be used is not particularly limited so long as it is used as a base in a common reaction, and there may be preferably used metal alkoxides such as sodium methoxide; an alkali metal carbonate such as sodium carbonate, potassium carbonate and lithium carbonate; an alkali metal hydroxide such as sodium hydroxide, potassium hydroxide, lithium hydroxide and

barium hydroxide; or ammonias such as aqueous ammonia and concentrated ammonia-methanol (organic bases also may be used, such as N-methylmorpholine, triethylamine, tripropylamine, tributylamine, diisopropylethylamine, dicyclohexylamine, N-methylpiperidine, pyridine, 4-pyrrolidinopyridine, picoline, 4-(N,N-dimethylamino)pyridine, 2,6-di(t-butyl)-4-methylpyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO) and 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU)).

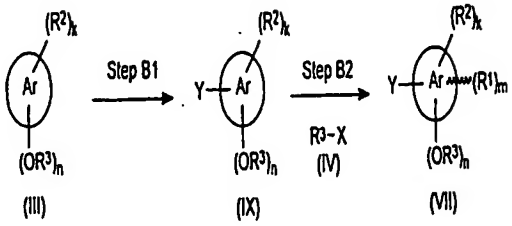
A reagent for introducing a tin atom is not particularly limited so long as it is a reagent used for introducing tin in a common reaction. Preferably, the tin containing compound is selected from a trialkyltin compound such as trimethyltin chloride, trimethyltin bromide, tripentyltin chloride, bis(trimethyltin) sulfide, bis(tributyltin) and bis(tributyltin)oxide; and a triphenyltin compound such as triphenyltin chloride and bis(triphenyltin)oxide.

The reaction temperature is 0°C to 200°C, preferably 50°C to 150°C.

The reaction time varies mainly depending on the reaction temperature and the kind of a starting compound, a reagent or a solvent to be used, and it is generally 1 hour to 5 days, preferably 5 to 10 hours.

Process B

Process B shown below is another process for preparing the compound having the formula (VII).



In the above formula, R1, R2, R3, X, Y, k, m and n have the same meanings as described above.

Step B1

Step B1 is a step of preparing a halogenated aryl compound (IX) by halogenating the compound having the formula (III), and is carried out according to Step A2.

Step B2

Step B2 is a step of preparing the compound having the formula (VII) by a condensation reaction of the halogenated aryl compound (IX) with the sugar derivative (IV), and is carried out according to Step A1.

After completion of the above respective reactions, the desired compound is collected from the reaction mixture according to a conventional method.

For example, the desired compound is obtained by neutralizing the reaction mixture suitably, or when insolubles exist, after the insolubles are removed by filtration, adding an organic solvent such as ethyl acetate which does not mix with water, washing the resulting mixture with water or the like, separating the organic layer containing the desired compound, drying the organic layer over anhydrous magnesium sulfate and then removing the solvent.

If necessary, the desired compound obtained can be separated and purified according to a conventional method, for example, by suitably combining recrystallization, reprecipitation and a method generally and conventionally used for separation and purification of an organic compound, for example, a method of using a synthetic adsorbent such as adsorption column chromatography using a silica gel, alumina or magnesium-silica gel type carrier such as Florisil; and partition column chromatography using a carrier such as Sephadex LH-20 (produced by Pharmacia Co.), Amberlite XAD-11 (produced by Rohm & Haas Co.) and Diaion HP-20 (produced by Mitsubishi Kasei Corporation), a method of using an ion exchange chromatograph, or normal phase or reverse phase column chromatography (preferably high performance liquid chromatography) using silica gel or alkylated silica gel, and eluting the desired compound by a suitable eluent.

The starting compounds are available as commercially available products or can be easily synthesized according to a known preparation process.

The C-glycosylated aryltin compound in the present invention can be converted into various C-glycosylated derivatives by reacting it various kinds of organic halides and equivalent compounds thereof in the presence of a palladium catalyst under mild conditions.

As the organic halides and equivalent compounds thereof, there may be mentioned acid halide, benzyl halide, allyl halide and acetate, vinyl halide and triflate, aryl halide, α-haloketone and α-haloester.

Further, in the reaction with benzyl halide, allyl halide and acetate, vinyl halide and triflate, aryl halide or the like in the presence of carbon monooxide, an insertion reaction of carbon monooxide occurs to give a corresponding derivative.

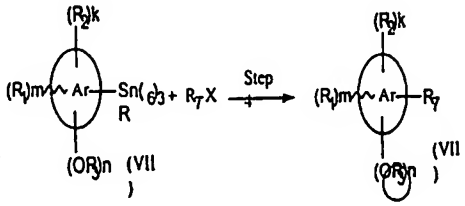
A palladium coupling reaction of a tin compound is described in detail in the introductions of the following literatures.

1). J.K. Still, Angew. Chem. Int. Ed. Engl., 25, 508, (1986)

2) T.N. Mitchell, Synthesis, 803 (1991)

Process C

The subject compounds can be synthesized in accordance with the following method:



In the above formulae R1, R2, R3, Ar, k, m and n are as defined above.

R6 represents lower alkyl group having 1 to 10 carbon atoms or phenyl group.

R7 represents aryl group substituted with nitro, ketone, ester, carboxy, nitrile, hydroxy, alkoxy, acyloxy, amine, amide, sulfonyl, sulfonamide, or straight, branched or cyclic alkyl groups with or without ketone, ester, carboxy groups; benzyl group substituted with nitro, ketone, ester, carboxy, nitrile, hydroxy, alkoxy, acyloxy, amine, amide, sulfone, sulfonamide, or straight, branched or cyclic alkyl groups with or without ketone, ester, carboxy groups; vinyl group substituted with nitro, ketone, ester, carboxy, niorile, hydroxy, alkoxy, acyloxy, amine, amide, sulfonyl, sulfonamide, or straight, branched or cyclic alkyl groups with or without ketone, ester, carboxy groups; allyl group substituted with

nitro, ketone, ester, carboxy, nitrile, hydroxy, alkoxy, acyloxy, amine, amide, sulfonyl, sulfonamide, or straight, branched or cyclic alkyl groups with or without ketone, ester, carboxy groups; or acyl groups.

X represents a leaving groups such as halogen atoms (fluorine, chlorine, bromine and iodine atoms), alkyl carbonyloxy groups (acetoxy, etylcarbonyloxy, propylcarbonyloxy etc.), lower alkanesulfonyloxy groups (methanesulfonyloxy, ethanesulfonyloxy etc.), lower haloalkanesulfonyloxy groups (trifluoromethanesulfonyloxy etc.)

There is no particular limitation on the palladium catalysts used in this Stille-type palladium mediated cross-coupling reactions. Any palladium catalysts commonly used in a coupling reaction of this type may be employed.

Examples of such catalysts include palladium(II) acetate, acetylacetonate, chloride, cyanide, trifluoroacetate, [1,2-bis-(diphenylphosphino)ethanedichloropalladium(II), bis(acetonitrile) dichloropalladium(II), bis(acetato) bis(triphenylphosphine) palladium(II), bis(benzonitorile) dichloropalladium(II), [1,libis(diphenylphosphino) ferrocene] dichloropalladium(II), (2,2i-bipyridine) dichloropalladium(II), (bicyclo[2,2,1] hepta-2,5-diene) dichloropalladium(II), dichloro(1,5-cyclooctadiene)palladium(II) dichlorobis (tri-phenylphosphine)palladium(0), tetrakis (triphenylphosphine)palladium(0), bis[1,2-bis (diphenylphosphino)ethane] palladium(0).

There is no particular limitation on the additives which are usually used on the purpose to enhance the reaction.

Examples of such additives include organic bases (triethylamine, diisopropylethylamine, 1,5-diazabicyclo[4,3,0]non-5-ene, 1,4-diazabicyclo[2,2,2]octane, 1.8-diazabicyclo[5,4,0]undecene, pyridine, lutidine, collidine etc.) or inorganic bases (sodium carbonate, potassium carbonate, sodium bicarbonate, potassium

bicarbonate etc.) or salts (lithium chloride, sodium acetate, copper(I) bromide, iodide, chloride or tetrabutyl ammoniumbromide etc.) or phosphine ligands (triphenylphosphine, tri-o-tolyphosphine, tributylphosphine, triphenylphosphite, tributylphosphite etc.) or radical scavenger (2,6-ditertbutyl-p-cresol etc.).

There is no particular limitation on the molar ratio of the palladium catalysts toward the compound represented by (Ar) and any ratio commonly used in this type reaction may equally be employed. An example of such ratio is 1:1 to 0.01:1 (catalyst: (Ar)).

This reaction is normally and preferably carried out in the presence of a solvent, the nature of which is not critical, provided that it has no adverse effect upon the reaction and that the solvent can dissolve the reagents, at least to some extent.

Examples of suitable solvents include aromatic hydrocarbons (benzene, toluene, xylene), esters (ethyl acetate, propyl acetate), ethers (tetrahydrofurane, dioxane, dimethoxyethane), nitriles (acetonitrile, isobutyronitrile), amides (formamide, dimethylformamide, dimethylacetamide), sulfoxides and sulfones (dimethylsulfoxide, sulfolene).

There is no particular limitation on the molar ratio of the compound represented by R^7 and the compound represented by Ar and any ratio commonly used in this type reaction may equally be employed. An example of such ratio is 1:1 to 5:1 (R^7: (Ar)).

The reaction can place over a wide range of temperature, and the precise reaction temperature chosen is not critical to the invention. In general, it is convenient to carry out the reaction at a temperature of from 0°C to 200°C, more preferably from 50°C to 150°C.

The time required for the reaction may likewise vary widely, depending on many factors, notably the reaction temperature, the starting materials, the solvent employed and the nature of the reagents. However, in most cases, a period of from 1 hour to 7 days, more preferably from 3 hours to 3 days, will normally suffice for the reaction.

Use And Administration

Although the compound of the present invention can be typically administered intravenously, orally, parenterally, or in the form of an implant, as a general rule, it can also be rectally administered. Examples of suitable solid or liquid forms of the preparation include granules, powders, tablets, coated enteric pills, microcapsules, suppositories, syrups, emulsions, suspensions, aerosols, drops, injection preparations in ampule form, as well as preparations in which release of the active compound is prolonged. Excipients, additives and/or auxiliaries are normally used in the manufacturing of these preparations, examples of which include disintegrating agents, binders, coating agents, swelling agents, lubricants, fragrances, sweeteners and solubilizing agents. Examples of bases or auxiliaries that are frequently used include magnesium carbonate, titanium dioxide, lactose, mannitol, other saccharides, talc, milk protein, gelatin, starch, vitamins, cellulose, its derivatives, animal oils, vegetable oils, polyethylene glycol and solvents such as sterile water, alcohols, glycerol and polyvalent alcohols.

The preparation of the compound of the present invention for administration is preferably manufactured in individual doses. Solid individual doses are in the form of tablets, capsules and suppositories. Different daily doses are respectively required in the treatment of the patient according to compound activity, dosing method, properties of the disease, condition, patient age and body weight. However, the daily dose

should be suitably increased or decreased depending on the specific circumstances. The dose for the compound of the present invention is preferably 1 to 500 mg/day and more preferably 10 to 300 mg/day.

Administration of a daily dose is performed either by administering once in a single dose unit or in the form of several smaller dose units, or by giving several administrations of smaller doses at specific intervals. The daily dose that is administered is additionally dependent on the number of receptors that appear during the course of the disease. In the early stage of a disease, since only a few receptors appear on the surface of cells, the daily dose that is administered is considered to be lower than that in the case of seriously ill patients. The compound of the present invention is suitable for the production of an antibody for diagnosis and measurement of ligands that are not easily approached, do not have sufficient immunoantigenicity or are unknown.

In numerous autoimmune diseases and tumors, a considerable number of specific ligands or antigens on the cell membrane are regulated. However, these are frequently unknown, are unable to be isolated in pure form, or do not have sufficient antigenicity to produce an antibody from them. The compound of the present invention can be used in the production of an antibody that cross-reacts with epitopes of natural ligands that are unknown or not easy to approach. Antibody produced in this manner is considered to be able to be used in both diagnosis and treatment (A.N., Houghton, D.A., Scheinberg, Semin. Oncol., 13, 165-179 (1986); W.C., Eckelmann, "*In vivo* Diagnosis and Treatment of Human Tumors Using Monoclonal Antibody,". Pergamon Press, London, (1988); M.H., Ravindranath, D.L., Morton, R.F., Irie, Cancer Res., 49, 3891-3897 (1989)).

The compound of the present invention can be used to treat and/or prevent the following diseases and conditions: rheumatoid arthritis, asthma, allergy, psoriasis, osteoarthritis, septic shock, transplanted tissue rejection reaction, reperfusion disorders, adult dyspnea syndrome, ischema, ulcerative colitis, atherosclerosis, thrombosis, ulcer, infections, cancer, cancer metastasis, wounds, osteoporosis, systemic lupus erythematosus, multiple sclerosis, myasthenia gravis, and diabetes mellitus.

The present invention will now be described by the following non-limiting examples.

Example 1

[3-(ß-L-Fucopyranosyl)-2-methoxyphenyl]acetic acid

Example 1(a)

Methyl 2-methoxy-3-(2,3,4-tri-O-acetyl-ß-L-fucopyranosyl) phenylacetate

Under an argon gas atmosphere, a 1M methylene chloride solution (9ml, 9mmol) of tin(IV) chloride was added to a reaction mixture of methyl 2-methoxy-phenylacetate (1.08g, 6mmol) , L-fucose 1,2,3,4-tetraacetate (996mg, 3mmol), and silver trifluoroacetate (990mg, 4.5mmol) in methylene chloride (30ml) at 0°C. After being stirred for 18 hours at room temperature, the reaction was quenched by adding water. The insoluble material was filtered off through a celite pad, and the filtrate was washed by a saturated aqueous solution of sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. Purification was carried out by column chromatography with ethyl acetate/hexane (1/3) which afforded 902mg (66.5%) of the titled compound.

Example 1(b)

[3-(β-L-Fucopyranosyl)-2-methoxyphenyl]acetic acid

To a methanol solution (30ml) of the above product was added a catalytic amount (0.1ml) of 28% sodium methoxide methanol solution. After being stirred for 2 hours, a 1N sodium hydroxide aqueous solution (4ml) was added to the reaction mixture and was stirred for 4 hours. The reaction mixture was acidified (pH 3) by adding a 1N aqueous solution of hydrogen chloride and the whole reaction mixture was concentrated under reduced pressure. A purification by column chromatography with 5% methanol-methylene chloride afforded 416mg (62.3%) of the titled compound.

$[\alpha]_D$ = -44.1 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.14 (1H, doublet of doublets, J=2.2, 8.8Hz),
7.04 (1H, doublet, J=2.2Hz),
6.82 (1H, doublet, J=8.8Hz),
3.94 (1H, doublet, J=9.5Hz),
3.71 (1H, quartet, J=6.6Hz),
3.66 (1H, doublet, J=3.7Hz),
3.63 (1H, triplet, J=9.5Hz),
3.63 (3H, singlet),
3.54 (1H, doublet of doublets, J=3.7, 9.5Hz),
3.28 (2H, singlet)
1.04 (3H, doublet, J=6.6Hz).

Example 2

[3,4-Dimethoxy-5-(β-L-fucocyranosyl)phenyl]acetic acid

Example 2(a)

Ethyl (3,4-dimethoxyphenyl)acetate

The mixture of (3,4-dimethoxyphenyl)acetic acid (25.7g) in ethanol (300ml), toluene (300ml) and sulfuric acid (2ml) was

refluxed for 24 hours. Solvent was removed by an evaporator and a saturated aqueous solution of sodium bicarbonate was added. The organic materials were extracted by ethyl acetate. The extract was dried over magnesium sulfate and solvent was removed under reduced pressure to give ethyl (3,4-dimethoxyphenyl)acetate (29.2g) without further purification.

Example 2(b)

[3,4-Dimethoxy-5-(β-L-fucopyranosyl)phenyl]acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and ethyl (3,4-dimethoxyphenyl)acetate (prepared using (3,4-dimethoxyphenyl)acetic acid as described in Example 2(a) above) to give ethyl [3,4-dimethoxy-5-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]acetate as a foam in a yield of 13%.

A procedure similar to that described in Example 1(b), above, was followed, but using etyl [3,4-dimethoxy-5-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]acetate to give the titled compound as a freeze-dried product in a yield of 70%.

$[\alpha]_D$ = -19 (c=0.1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.22 (singlet, 1H),
6.92 (singlet, 1H),
4.49 (doublet, J=9.5Hz, 1H),
3.90, 3.88 (2 x singlet, 6H),
3.97-3.85 (multiplet, 3H),
3.81 (doublet of doublets, J=3.5, 9.5Hz, 1H),
3.65 (doublet, J=16.0Hz, 1H),
3.56 (doublet, J=16.0Hz, 1H),
1.25 (doublet, J=6.5Hz, 3H).

Example 3

2-[5-(β-L-Fucopyranosyl)-6-methoxynaphthalen-2-yl]propionic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 2-(6-methoxynaphthalen-2-yl)propionate (prepared using 2-(6-methoxynaphthalen-2-yl) propionic acid as described in Example 2(a) above), to give methyl 2-[6-methoxy-5-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)naphthlen-2-yl] propionate as a foam in a yield of 57%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 2-[6-methoxy-5-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)naphthalen-2-yl] propionate as to give the titled compound as a freeze-dried product in a yield of 71%.

$[\alpha]_D$ = +0.40 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

8.54 (doublet, J=9.1Hz, 1H),
7.96 (doublet, J=9.1Hz, 1H),
7.79 (singlet, 1H),
7.51 (doublet of doublets, J=1.9, 9.1Hz, 1H),
7.45 (doublet, J=9.1Hz, 1H),
5.32 (doublet, J=9.8Hz, 1H),
4.42 (triplet, J=9.8Hz, 1H),
3.96 (singlet, 3H),
4.03-3.92 (multiplet, 2H),
3.85-3.75 (multiplet, 2H),
1.51 (doublet, J=7.3Hz, 3H),
1.32 (dobulet, J=6.5Hz, 3H).

Example 4

[2-(β -L-Fucopyranosyl)-3,4,5-trimethoxyphenyl]acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl (3,4,5-trimethoxyphenyl) acetate (prepared using (3,4,5-trimethoxyphenyl) acetic acid as described in Example 2(a) above) to give methyl [2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-3,4,5- trimethoxyphenyl] acetate as a foam in a yield of 29%.

A proceedure similar to that described in Example 1(b) above was followed, but using methyl [2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-3,4,5-trimethoxyphenyl]acetate to give the titled compound as a freeze-dried product in a yield of 74%.

$[\alpha]_D$ = -17 (c=0.2, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

6.78 (singlet, 1H),
4.48-4.35 (multiplet, 1H),
3.89 (singlet, 3H),
3.87 (2 x singlet, 6H)
4.10-3.73 (multiplet, 3H),
3.73-3.53 (multiplet, 3H),
1.26 (doublet, J=6.3Hz, 3H).

Example 5

[3-(β-L-Fucopyranosyl)-4-methoxyphenyl]acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and etyl (4-methoxyphenyl) acetate to give ethyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] acetate as a foam in a yield of 59%.

A procedure similar to that described in Example 1(b) above was followed, but using ethyl [4-methoxy-3-(2,3,4-tri-O-

acetyl-β-L-fucopyranosyl)phenyl] acetate to give the titled compound as a freeze-dried product in a yield of 80%.

$[\alpha]_D$ = -22.6 (c=1.35, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.14 (doublet of doublets, J=2.2, 8.8Hz, 1H),
7.04 (doublet, J=2.2Hz, 1H),
6.82 (doublet, J=8.8Hz, 1H),
3.94 (doublet, J=9.5Hz, 1H),
3.71 (quartet, J-6.6Hz, 1H),
3.66 (doublet, J=3.7Hz, 1H),
3.63 (triplet, J=9.5Hz, 1H),
3.63 (singlet, 3H),
3.54 (doublet of doublets, J=3.7, 9.5Hz, 1H),
1.04 (doublet, J=6.6Hz, 3H).

Example 6

[4-(α -L-Fucopyranosyl)-3-methoxyphenyl]acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and ethyl(4-methoxyphenyl)acetate (prepared using (3-methoxyphenyl) acetic acid as described in Example 2(a) above) to give ethyl [3-methoxy-4-(2,3,4-tri-O-acetyl-α-L-fucopyranosyl)phenyl]acetate as a foam in a yield of 14%.

A procedure similar to that described in Example 1(b) above was followed, but using ethyl [3-methoxy-4-(2,3,4-tri-O-acetyl-α -L-fucopyranosyl)phenyl]acetate to give the titled compound as a freeze-dried product in a yield of 78%.

$[\alpha]_D$ = +20.0 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400 MHz, WEFT, D_2O) δ ppm:

7.23(doublet, J=8.1Hz, 1H),
6.79(doublet, J=1.5Hz, 1H),

6.72(doublet of doublets, J=1.5, 8.1Hz, 1H),
5.27(doublet, J=3.7Hz, 1H),
3.98(doublet of doublets, J=3.7, 5.9Hz, 1H),
3.93-3.82(multiplet, 3H),
3.65(singlet, 3H),
3.47(singlet, 2H),
1.11(doublet, J=6.6Hz, 3H).

Example 7

1-[3-(β-L-Fucopyranosyl)-4-methoxyphenyl] cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above), to give methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexanecarboxylate as a foam in a yield of 89%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-fucopyranosyl) phenyl]cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 36%.

$[\alpha]_D$, = -20.3 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.34 (doublet, J=2.4Hz, 1H),
7.22 (doublet of doublets, J=2.4, 8.8Hz, 1H),
6.85 (doublet, J=8.8Hz, 1H),
4.50 (doublet, J=9.8Hz, 1H),
3.74 (triplet, J=9.8Hz, 1H),
3.72 (quartet, J=6.4Hz, 1H),
3.67 (doublet, J=3.4Hz, 1H),

3.63 (singlet, 3H),
3.56 (doublet of doublets, J=3.4, 9.8Hz, 1H),
2.14-2.02 (multiplet, 2H),
1.60-1.19 (multiplet, 7H),
1.04 (doublet, J=6.4Hz, 3H),
1.16-1.02 (multiplet, 1H).

Example 8

2-[4-(α-L-Fucopyranosyl)-3-methoxyphenyl] propionic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 2-(3-methoxyphenyl)propionate (prepared using 2-(3-methoxyphenyl)propionic acid as described in Example 2(a) above), to give methyl 2-[3-methoxy-4-(2,3,4-tri-O-acetyl-α-L-fucopyranosyl) phenyl]propionate as a foam in a yield of 19%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 2-[3-methoxy-4-(2,3,4-tri-O-acetyl-α-L-fucopyranosyl) phenyl]propionate to give the titled compound as a freeze-dried product in a yield of 72%.

$[\alpha]_D$ = +16.2 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.21 (doublet, J=8.1Hz, 1H),
6.81 (singlet, 1H),
6.76 (doublet, J=8.1Hz, 1H),
5.27 (doublet, J=3.7Hz, 1H),
4.00 (doublet of doublets, J=3.7, 6.6Hz, 1H),
3.94-3.78 (multiplet, 3H),
3.67 (singlet, 3H),
3.45 (quartet, J=7.3Hz, 1H),
1.21 (doublet, J=7.3Hz, 3H),
1.10 (doublet, J=6.6Hz, 3H).

Example 9

3-[3-(β-L-fucopyranosyl)-4-methoxyphenyl] propionic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 3-(4-methoxyphenyl)propionate [prepared using 3-(4 methoxyphenyl)propionic acid as described in Example 2(a), above], to give methyl 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl]propionate as a foam in a yield of 91%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] propionate to give the titled compound as a freeze-dried product in a yield of 85%.

$[\alpha]_D$ = 13.4 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.17 (doublet, J=2.2Hz, 1H),
7.05 (doublet of doublets, J=2.2, 8.8Hz, 1H),
6.81 (doublet, J=8.8Hz, 1H),
4.49 (doublet, J=9.5Hz, 1H),
3.73 (triplet, J=9.5Hz, 1H),
3.71 (quartet, J=6.6Hz, 1H),
3.67 (doublet, J=3.7Hz, 1H),
3.62 (singlet, 3H),
3.56 (doublet of doublets, J=3.7, 9.5Hz, 1H),
2.65 (triplet, J=7.3Hz, 2H),
2.29 (triplet, J=7.3Hz, 2H),
1.04 (doublet, J=6.6Hz, 3H).

Example 10

[3-(β-D-Ribofuranosyl)-4-methoxyphenyl]acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using β-D-ribofuranose 1,2,3,5-

tetraacetate and ethyl (4-methoxyphenyl) acetate to give ethyl (4-methoxy-3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)phenyl] acetate as a foam in a yield of 21%.

A procedure similar to that described in Example 1(b) above was followed, but using ethyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β -D-ribofuranosyl)phenyl] acetate to give the titled compound as a freeze-dried product.

$[\alpha]_D$ = -31.9 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.17 (doublet, J=2.2Hz, 1H),
7.05 (doublet of doublets, J=2.2, 8.1Hz, 1H),
6.83 (doublet, J=8.1Hz, 1H),
5.20 (doublet, J=2.9Hz, 1H),
4.28 (doublet of doublets, J=2.9, 4.4Hz, 1H),
4.17 (doublet of doublets, J=4.4, 8.8Hz, 1H),
3.91-3.87 (multiplet, 1H),
3.74 (doublet of doublets, J=2.9, 12.5Hz, 1H),
3.64 (singlet, 3H),
3.56 (doublet of doublets, J=5.1, 12.5Hz, 1H),
3.50 (singlet, 2H).

Example 11

[3-(β -L-fucopyranosyl)-4-methoxyphenoxy]acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl (4-methoxyphenoxy)acetate to give methyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenoxy]acetate as a foam in a yield of 65%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenoxy]acetate to give the titled compound as a freeze-dried product in a yield of 63%.

$[\alpha]_D$ = -17.2 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

6.89 (doublet, J=2.9Hz, 1H),
6.86 (doublet, J=8.8Hz, 1H),
6.74 (doublet of doublets, J=2.9, 8.8Hz, 1H),
4.49 (doublet, J=9.5Hz, 1H),
4.27 (singlet, 2H),
3.77-3.65 (multiplet, 3H),
3.61 (singlet, 3H),
3.56 (doublet of doublets, J=3.7, 9.5Hz, 1H),
1.05 (doublet, J=6.6Hz, 3H).

Example 12

4-[3-β -L-Fucopyranosyl)-4-methoxyphenyl]butyric acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl (4-methoxyphenyl)butyrate (prepared using (4-methoxyphenyl)butyric acid as described in Example 2(a) above), to give methyl 4-[4-methoxy-3-(2,3,4-tri-O-acetyl-β -L-fucopyranosyl) fucopyranosyl) phenyl] butyrate as an oil in a yield of 82%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 4-[4-methoxy-3-(2,3,4-tri-O-acetyl-β -L-fucopyranosyl) phenyl] butyrate to give the titled compound as a freeze-dried product in a yield of 69%.

$[\alpha]_D$ = -11.8 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.18 (doublet, J=2.2Hz, 1H),
7.06 (doublet of doublets, J=2.2, 8.8Hz, 1H)
6.83 (doublet, J=8.8Hz, 1H)
4.49 (doublet, J=10.3Hz, 1H),
3.74 (triplet, J=10.3Hz, 1H),
3.72 (quartet, J=6.6Hz, 1H)

3.67 (doublet, J=2.9Hz, 1H),
3.63 (singlet, 3H)
2.56 (doublet of doublets, J=2.9, 10.3Hz, 1H)
2.40 (triplet, J=7.3Hz, 2H),
2.00 (triplet, J=7.3Hz, 2H),
1.72-1.60 (multiplet, 2H),
1.04 (doublet, J=6.6Hz, 3H)

Example 13

4-[β-L-Fucopyranosyl)-7-methoxybenzofuran-2-carboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 7-methoxybenzofuran-2-carboxylate (prepared using 7-methoxybenzofuran-2-carboxylic acid as described in Example 2(a) above), to give methyl 7-methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzofuran-2-carboxylate as a foam in a yield of 59%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 7-methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) benzofuran-2-carboxylate to give the titled compound as a freeze-dried product in a yield of 66%.

$[\alpha]_D$ = -12.0 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.33 (singlet, 1H),
7.15 (doublet, J=8.1Hz, 1H),
6.88 (doublet, J=8.1Hz, 1H)
4.33 (doublet, J=9.5Hz, 1H)
3.84 (singlet, 3H),
3.89-3.74 (multiplet, 2H),
3.73 (doublet, J=3.7Hz, 1H),
3.63 (doublet of doublets, J=3.7, 9.5Hz, 1H)
1.07 (doublet, J=5.9Hz, 3H)

Example 14

1-[3-β -D-Fucopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using D-fucose 1,2,3,4-tetraacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above), to give methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β -D-fucopyranosyl) phenyl] cyclohexanecarboxylate as a foam in a yield of 31%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β -D-fucopyranosyl) phenyl] cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 85%.

$[\alpha]_D$ = +9.2 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.37 (doublet, J=2.2Hz, 1H),
7.25 (doublet of doublets, J=2.2, 8.8Hz, 1H),
6.88 (doublet, J=8.8Hz, 1H),
4.52 (doublet, J=9.5Hz, 1H),
3.74-3.66 (multiplet, 1H),
3.71 (triplet, J=9.5Hz, 1H),
3.68 (doublet, J=2.9Hz, 1H),
3.64 (singlet, 3H),
3.57 (doublet of doublets, J=2.9, 9.5Hz, 1H),
2.15 (doublet, J=13.2Hz, 2H),
1.64 (triplet, J=11.0Hz, 2H),
1.48-1.39 (multiplet, 3H),
1.31-1.22 (multiplet, 2H),
1.15-1.04 (multiplet, 1H),
1.04 (doublet, J=6.6Hz, 3H).

Example 15

1-[4-Methoxy-3-(β -D-ribopyranosyl]) phenyl] cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using β-D-ribopynanose 1,2,3,4-tetraacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above), to give methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-D-ribopyranosyl]phenyllcyclohexanecarboxylate as a foam in a yield of 23%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-D-ribopyranosyl)phenyl]cyclohexanecarboxylate to give the titled compound as a freeze-dried product.

$[\alpha]_D$ = -3.0 (c=0.3, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.27 (singlet, 1H),
7.24 (doublet, J=8.8Hz, 1H),
6.86 (doublet, J=8.8Hz, 1H),
4.70 (doublet, J=10.3Hz, 1H),
4.09 (triplet, J=2.9Hz, 1H),
3.87 (doublet of doublets, J=2.9, 10.3Hz, 1H),
3.79 (doublet of doublet of doublets, J=2.9, 5.1, 11.0Hz, 1H),
3.65 (singlet, 3H),
3.58 (doublet of doublets, J=5.1, 11.0Hz, 1H),
3.49 (triplet, J=11.0Hz, 1H),
2.05 (doublet, J=13.2Hz, 2H),
1.54-1.06 (multiplet, 8H).

Example 16

1-[3-β -D-Galactopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using β-D-galactose 1,2,3,4,6-pentaacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl 1-[4-methoxy-3-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)phenyl]cyclohexanecarboxylate as a foam in a yield of 12%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4,6-tetra-O-acetyl-β -D-galactopyranosyl)phenyl]cyclohexanecarboxylate to give the titled compound as a foam in a yield of 86%.

$[\alpha]_D$ = +25.4 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.34 (doublet, J=2.4Hz, 1H),
7.22 (doublet of doublets, J=2.4, 8.8Hz, 1H),
6.85 (doublet, J=8.8HZ, 1H),
4.51 (doublet, J=9.8Hz, 1H),
3.87 (doublet, J=2.9Hz, 1H),
3.78 (triplet, J=9.8Hz, 1H),
3.64 (singlet, 3H),
3.68-3.50 (multiplet, 4H),
2.11-2.00 (multiplet, 2H),
1.57-1.19 (multiplet, 7H),
1.15-1.02 (multiplet, 1H).

Example 17

1-[3-(β -D-glucopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using β-D-glucose 1,2,3,4,6-pentaacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above), to give methyl 1-[4-methoxy-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)phenyl]cyclohexanecarboxylate as a foam in a yield of 5%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4,6-tetra-O-acetyl-β -D-glucopyranosyl)phenyl]cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 72%.

$[\alpha]_D$ = +9.0 (c=0.2, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.26 (doublet, J=2.4Hz, 1H),
7.23 (doublet of doublets, J=2.4, 8.8Hz, 1H),
6.86 (doublet, J=8.8Hz, 1H),
4.53 (doublet, J=9.8Hz, 1H),
3.64 (singlet, 3H),
3.70-3.51 (multiplet, 3H),
3.45-3.30 (multiplet, 3H),
2.10-1.98 (multiplet, 2H),
1.56-1.18 (multiplet, 7H),
1.15-1.02 (multiplet, 1H).

Example 18

1-[4-Methoxy-3-(β-L-rhamnopyranosyl) phenyl] cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-rhamnose 1,2,3,4-tetraacetate

and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyohenyl)cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)phenyl]cyclohexanecarboxylate as a foam in a yield of 83%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β -L-rhamnopyranosyl)phenyl]cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 58%.

$[\alpha]_D$ = -26.1 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.30 (doublet, J=2.4Hz, 1H),
7.16 (doublet of doublets, J=2.4, 8.8Hz, 1H),
6.81 (doublet, J=8.8Hz, 1H),
4.78 (singlet, 1H),
3.83 (doublet, J=3.4Hz, 1H),
3.63 (singlet, 3H),
3.58 (doublet of doublets, J=3.4, 9.3Hz, 1H),
3.38-3.26 (multiplet, 2H),
2.08-1.98 (multiplet, 2H),
1.18 (doublet, J=5.9Hz, 3H),
1.57-1.02 (multiplet, 8H).

Example 19

1-[4-methoxy-3-(β-D-xylopyranosyl)phenyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using D-xylose 1,2,3,4-tetraacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl

1-[4-methoxy-3-(2,3,4-tri-o-acetyl-β-D-xylopyranosyl)phenyl] cyclohexanecarboxylate as a foam in a yield of 62%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl) phenyl]cyclohexanecarboxylate to give the titled compound as a white solid in a yield of 62%.

$[\alpha]_D$ = -10.1 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT,) D_2O) δ ppm:
7.24 (doublet of doublets, J=2.4, 8.8Hz, 1H),
7.20 (doublet, J=2.4Hz, 1H),
6.85 (doublet, J=8.8Hz, 1H),
4.43 (doublet, J=9.8Hz, IH),
3.82 (doublet of doublets, J=5.4, 11.2Hz, 1H),
3.63 (singlet, 3H),
3.67-3.52 (multiplet, 2H),
3.35 (triplet, J=8.8Hz, 1H),
3.23 (triplet, J=11.2Hz, 1H),
2.10-1.97 (multiplet, 2H),
1.57-1.19 (multiplet, 7H),
1.16-1.02 (multiplet, 1H).

Example 20

1-[3-(β-L-Fucopyranosyl)-4-methoxyphenyl]cyclopentanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-(4-methoxyphenyl)cyclopentanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclopentanecarboxylic acid as described in Example 2(a) above) to give methyl 1-(4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl]cyclopentanecarboxylate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β -L-fucopyranosyl) phenyl]cyclopentanecarboxylate to give the titled compound as a freeze-dried product in a yield of 39%.

$[\alpha]_D$ = -30.1 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.27 (doublet, J=2.4HZ, 1H),
7.17 (doublet of doublets, J=2.4, 8.8Hz, 1H),
6.83 (doublet, J=8.8Hz, 1H),
4.49 (doublet, J=9.8Hz, 1H),
3.67 (doublet, J=3.4Hz, 1H),
3.81-3-65 (multiplet, 2H),
3.63 (singlet, 3H),
3.56 (doublet of doublets, J=3.4, 9.8Hz, 1H),
2.22-2.12 (multiplet, 2H),
1.72-1.60 (multiplet, 2H),
1.51-1.40 (multiplet, 4H),
1.04 (doublet, J=6.4Hz, 3H).

Example 21

2-[3-(β-L-Fucopyranosyl)-4-methoxyphenyl]-2-methylpropionic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 2-(4-methoxyphenyl)-2-methylpropionate (prepared using 2-(4-methoxyphenyl)-2-methylpropionic acid as described in Example 2(a) above) to give methyl 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyll-2-methylpropionate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]-2-

methylpropionate to give the titled compound as a freeze-dried product in a yield of 52%.

$[\alpha]_D$ = -28.2 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.28 (doublet, J=2.4Hz, 1H),
7.16 (doublet of doublets, J=2.4, 8.8Hz, 1H),
6.85 (doublet, J=8.8Hz, 1H),
4.51 (doublet, J=6.8Hz, 1H),
3.67 (doublet, J=3.4Hz, 1H),
3.78-3.66 (multiplet, 2H),
3.64 (singlet, 3H),
3.57 (doublet of doublets, J=3.4, 9.8Hz, 1H),
1.30, 1.29 (2 x singlet, 6H),
1.04 (doublet, J=6.8Hz, 3H).

Example 22

1-[2-3-(β-L-Fucopyranosyl)-4-methoxyphenyl]ethyl)cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-[2-(4-methoxyphenyl)ethyl]cyclohexanecarboxylate (prepared using 1-[2-(4-methoxyphenyl) ethyl] cyclohexane-carboxylic acid as described in Example 2(a) above) to give methyl 1-{2-[4-methoxy-3-(2,3,4-tri-O-acetyl -β-L-fucocopyranosyl)phenyl]ethyl} cyclohexanecarboxylate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-{2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl]ethyl}cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 79%.

$[\alpha]_D$ = -5.6 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.37 (doublet, J=2.0Hz, 1H),
7.25 (doublet of doublets, J=2.0, 8.3Hz, 1H),
7.02 (doublet, J=8.3Hz, 1H),
4.69 (doublet, J=9.8Hz, 1H),
3.88 (doublet, J=3.4Hz, 1H),
3.98-3.86 (multiplet, 2H),
3.83 (singlet, 3H),
3.77 (doublet of doublets, J=3.4, 9.8Hz, 1H),
2.54-2.43 (multiplet, 2H),
2.00-1.90 (multiplet, 2H),
1.73-1.62 (multiplet, 2H),
1.62-1.48 (multiplet, 3H),
1.25 (doublet, J=6.3Hz, 3H),
1.42-1.20 (multiplet, 5H).

Example 23

1-[5-(β -L-Fucopyranosyl)-6-methoxynaphthalene-2-yl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-(6-methoxynaphthalene-2-yl)cyclohexanecarboxylate (prepared using 1-(6-methoxynaphthalene-2-yl) cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl 1-[6-methoxy-5-(2,3,4-tri-O- acetyl-β-L-fucopyranosyl) naphthalene-2-yl]cyclohexanecarboxylate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-{6-methoxy -5-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) naphthalene-2-yl]cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 70%.

$[\alpha]_D$ = +5.9 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

8.32 (doublet, J=9.3Hz, 1H),
7.75 (doublet, J=9.3Hz, 1H),
7.67(doublet, J=2.0Hz, 1H),
7.43(doublet of doublets, J=2.0, 9.3Hz, 1H),
7.23(doublet, J=9.3Hz, 1H),
5.10(doublet, J=9.8Hz, 1H),
4.20(triplet, J=9.8Hz, 1H),
3.74(singlet, 3H),
3.83-3.72 (multiplet, 2H),
3.61(doublet of doublets, J=3.4, 9.8Hz, 1H),
2.22-2.08 (multiplet, 2H),
1.70-1.53 (multiplet, 2H),
1.53-1.25 (multiplet, 5H),
1.10 (doublet, J=6.3Hz, 3H),
1.19-1.06 (multiplet, 1H).

Example 24

3-[3-β-L-Fucopyranosyl)-4-methoxyphenyl]cyclohex-4-ene-1,2-dicarboxylic acid

To a suspension of allyltriphenylphosphonium bromide (6.65g) in tetrahydrofuran (THF) (40ml) was added n-butyl lithium hexane solution (1.66M, 11.5ml) dropwise at -78°C under a nitrogen atmosphere. The mixture was warmed up to -20°C. After 0.5 hours, the mixture was cooled to -50°C and p-anisaldehyde (2ml) was added. The mixture was stirred at -20°C for 2 hours and at room temperature for 0.5 hours. An aqueous solution of ammonium chloride was added and organic materials were extracted with dichloromethane and dried over anhydrous magnesium sulfate. A purification involving column chromatography afforded 1-buta-1,3-dienyl-4-methoxybenzene (1.99g). To the solution of the obtained 1-buta-1,3-dienyl-4-methoxybenzene (965mg) and dimethyl maleate (0.75ml) in toluene was added diethyl aluminum chloride hexane

solution (0.97M, 16.2ml) at -50°C under a nitrogen atmosphere. After 3 hours, an aqueous hydrochloric acid solution was added. The organic materials were extracted by ether and dried by magnesium sulfate. A purification by column chromatography (hexane:ethyl acetate = 3:1) afforded dimethyl 3-(4-methoxyphenyl)cyclohex-4-ene-1,2-dicarboxylate (711mg) in a yield of 39%.

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and dimethyl 3-(4-methoxyphenyl)cyclohex-4-ene-1,2-dicarboxylate (prepared as described in the preceding paragraph to give dimethyl 3-(4-methox-y-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl]cyclohex-4-ene-1,2-dicarboxylate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using dimethyl 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] cyclohex-4-ene-1,2-dicarboxylate to give the titled compound as a freeze-dried compound in a yield of 11%.

$[\alpha]_D$ = -17 (c=0.03, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2C) δ ppm:
7.10 (singlet, 1H),
7.00-6.95 (multiplet, 1H),
6.83-6.79 (multiplet, 1H),
5.72 (doublet, J=10.7Hz, 1H),
5.42 (doublet, J=10.7Hz, 1H),
5.27 (doublet, J=2.9Hz, 1H),
4.03-3.80 (multiplet, 4H),
3.65 (singlet, 3H),
3.28 (singlet, 1H),
2.62-2.04 (multiplet, 4H),
1.14 (doublet, J=5.4Hz, 3H).

Example 25

Diastereomer at 1,2 and 3 positions of Example 24 yield: 6.7%

$[\alpha]_D$, = +5.9 (c=1.1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.16 (singlet, 1H),
7.01-6.98 (multiplet, 1H),
6.83-6.80 (multiplet, 1H),
5.72 (doublet, J=10.3Hz, 1H),
5.43 (doublet, J=10.3Hz, IH),
4.50 (doublet, J=9.8Hz, 1H),
3.76-3.64 (multiplet, 3H),
3.65 (singlet, 3H),
3.56 (doublet of doublets, J=3.4, 9.8Hz, 1H),
3.27 (singlet, 1H),
2.60-2.03 (multiplet, 4H),
1.04 (doublet, J=6.8Hz, 3H).

Example 26

1-[3-(α-L-Fucopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-(4-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(4-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-α-L-fucopyranosyl)phenyl] cyclohexanecarboxylate as a foam in a yield of 11%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-α-L-fucopyranosyl)phenyllcyclohexanecarboxylate to give the titled compound as a freeze-dried compound in a yield of 85%.

$[\alpha]_D$ = +8.3 (c=0.29, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.33 (doublet, J=2.5Hz, 1H),
7.21 (doublet of doublets, J=2.5, 8.8Hz, 1H),
6.85 (doublet, J=8.8Hz, 1H),
5.28 (doublet, J=3.4Hz, 1H),
3.97 (doublet of doublets, J=3.4, 5.9Hz, 1H),
3.89 (quartet, J=6.4Hz, 1H),
3.86 (doublet, J=3.4Hz, 1H),
3.85 (doublet of doublets, J=3.4, 5.9Hz, 1H),
3.64 (singlet, 3H),
2.08 (doublet, J=12.7HZ, 2H),
1.56-1.05 (multiplet, 8H),
1.12 (doublet, J=6.4Hz, 3H).

Example 27

1-[3-β -L-Fucopyranosyl)-4-methoxybenzyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-(4-methoxybenzyl)cyclohexanecarboxylate (prepared using 1-(4-methoxybenzyl)cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl] cyclohexanecarboxylate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl] cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 55%.

$[\alpha]_D$ = -32.7 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.03 (doublet, J=2.4Hz, 1H),
6.95 (doublet of doublets, J=2.4, 8.3Hz, 1H),

6.78 (doublet, J=8.3Hz, 1H),
4.45 (doublet, J=9.8Hz, 1H),
3.66 (doublet, J=3.4Hz, 1H),
3.79-3.64 (multiplet, 2H),
3.62 (singlet, 3H),
3.55 (doublet of doublets, J=3.4, 9.8Hz, 1H),
2.51 (doublet, J=15.6Hz, 1H),
2.48 (doublet, J=15.6Hz, 1H),
1.73-1.58 (multiplet, 2H),
1.42-1.27 (multiplet, 3H),
1.04 (doublet, J=6.4Hz, 3H),
1.13-0.93 (multiplet, 5H).

Example 28

3-[3-β -L-Fucopyranosyl)-4-methoxyphenyl]glutaric acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and dimethyl 3-(4-methoxyphenyl)glutarate (prepared using 3-(4-methoxyphenyl)glutaric acid as described in Example 2(a) above) to give dimethyl 3-[4-methoxy-3- (2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] glutarate as a foam.

A procedure similar to that described in Example 1(b), above, was followed, but using dimethyl 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]glutarate to give the titled compound as a freeze-dried product in a yield of 90%.

$[\alpha]_D$ = -6.3 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT,]D_2O) δ ppm:
7.19 (doublet, J=1.5Hz, 1H),
7.06 (doublet of doublets, J=1.5, 8.3Hz, 1H),
6.81 (doublet, J=8.3Hz, 1H),
4.49 (doublet, J=9.8Hz, 1H),
3.62 (singlet, 3H),

3.55 (doublet of doublets, J=3.4, 9.8Hz, 1H),
3.82-3.49 (multiplet, 3H),
3.26-3.11 (multiplet, 1H),
2.43-2.15 (multiplet, 4H),
1.04 (doublet, J=6.8Hz, 3H).

Example 29

2-[3-(β -L-Fucopyranosyl)-4-methoxyphenyl]succinic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 2-(4-methoxyphenyl)succinate (prepared as using 2-(4-methoxyphenyl)succinic acid described in Example 2(a) above) to give dimethyl 2-(4-methoxy-3-(2,3,4-tri-O-acetyl-β -L-fucopyranosyl)phenyl]succinate as a foam.

A procedure similar to that described in Example 1(b) above was followed, but using dimethyl 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl] succinate to give the titled compound as a freeze-dried compound in a yield of 51%.

$[\alpha]_D$ = -3.9 (c=0.61, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.25-7.03 (multiplet, 2H),
6.90-6.79 (multiplet, 1H),
4.49 (doublet, J=9.8Hz, 1H),
3.65 (singlet, 3H),
4.05-3.50 (multiplet, 5H),
2.72-2.34 (multiplet, 2H),
1.12 (doublet, J=6.4Hz, 3H).

Example 30

1-[4-(β -L-Fucopyranosyl)-3-methoxyphenyl]cyclohexanecarboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 1-(3-methoxyphenyl)cyclohexanecarboxylate (prepared using 1-(3-methoxyphenyl)cyclohexanecarboxylic acid as described in Example 2(a) above) to give methyl 1-[3-methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] cyclohexanecarboxylate as crystals.

A procedure similar to that described in Example 1(b), above was followed, but using methyl 1-[3-methoxy-4-(2,3,4-tri-O-acetyl-β -L-fucopyranosyl)phenyl]cyclohexanecarboxylate to give the titled compound as a freeze-dried product in a yield of 60%.

$[\alpha]_D$ = -7.0 (c=1, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.29 (doublet, J=8.3Hz, 1H),
6.98 (doublet of doublets, J=1.5, 8.3Hz, 1H),
6.92 (singlet, 1H),
4.51 (doublet, J=9.8Hz, 1H),
3.68 (singlet, 3H),
3.79-3.64 (multiplet, 3H),
3.58 (doublet of doublets, J=3.4, 9.8Hz, 1H),
2.25-2.11 (multiplet, 2H),
1.05 (doublet, J=6.4Hz, 3H),
1.72-1.01 (multiplet, 8H).

Example 31

1,4-Dimethoxy-2-(β-D-galactopyranosyl)benzene

A procedure similar to that described in Example 1(a) above was followed, but using D-β-galactose 1,2,3,4,6-pentaacetate and 1,4-dimethoxybenzene to give

1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β -D-galacto-pyranosyl)benzene as a foam in a yield of 55%.

A procedure similar to that described in the first half of Example 1(b) above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl) benzene to give the titled compound as a foam in a yield of 85%.

$[\alpha]_D$ = +21 (c=0.40, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

6.97 (doublet, J=3.4Hz, 1H),
6.88 (doublet, J=9.3Hz, 1H),
6.81 (doublet of doublets, J=3.4, 9.3Hz, 1H),
4.52 (doublet, J=9.8Hz, 1H),
3.87 (doublet of doublets, J=1.0, 3.4Hz, 1H),
3.71 (triplet, J=9.8Hz, 1H),
3.63-3.60 (multiplet, 1H),
3.62-3.63 (2 x singlet, 6H),
3.58 (doublet of doublets, J=3.4, 9.8Hz, 1H),
3.55 (doublet, J=5.9Hz, 2H).

Example 32

5-(β-L-Fucopyranosyl)-6-methoxynaphthalene-1-carboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 6-methoxynaphthalene-1-carboxylate prepared using 6-methoxynaphthalene-1-carboxylic acid as described in Example 2(a) above) to give methyl 6-methoxy-5-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)naphthalene-1-carboxylate as a foam in a yield of 72%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 6-methoxy-5-(2,3,4-tri-O-acetyl-β-L-fucozyranosyl)

naphthalene-1-carboxylate to give the titled compound as a freeze-dried product in a yield of 80%.

$[\alpha]_D$ = -11 (c=0.20, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

8.39 (doublet, J=8.3Hz, 1H),
8.01 (doublet, J=9.8Hz, 1H),
7.39-7.24 (multiplet, 3H),
5.16 (doublet, J=9.8Hz, 1H),
4.22 (triplet, J=9.8Hz, 1H),
3.82-3.78 (multiplet, 2H),
3.77 (singlet, 3H),
3.62 (doublet of doublets, J=3.4, 9.8Hz, 1H),
1.11 (doublet, J=6.4Hz, 3H).

Example 33

4,4'-Dimethoxy-3'-(β-L-Fucopyranosyl)biphenyl-3-yl-oxo-acetic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 4,4'-dimethoxybiphenyl-3-yl-oxo-acetate (prepared using 4,4'-dimethoxybiphenyl-3-yl-oxo-acetic acid as described in Example 2(a) above) to give methyl 4,4'- dimethoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) biphenyl-3-yl-oxo-acetate as a foam in a yield of 65%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 4,4'-dimethoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-3-yl-oxo-acetate to give the titled compound as a freeze-dried product in a yield of 76%.

$[\alpha]_D$ = -0.7 (c=1.0, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

8.04 (doublet, J=2.6Hz, 1H),
7.94 (doublet of doublets, J=2.6, 8.8Hz, 1H),

7.86 (doublet, J=2.3Hz, 1H),
7.53 (doublet of doublets, J=2.3, 8.4Hz, 1H),
7.22 (doublet, J=8.8Hz, 1H),
7.06 (doublet, J=8.4Hz, 1H),
4.72 (doublet, J=9.6Hz, 1H),
3.92 (singlet, 3H),
3.88 (triplet, J=9.6Hz, 1H),
3.86 (singlet, 3H),
3.80 (quartet, J=6.3Hz, 1H),
3.75 (doublet, J=3.5Hz, 1H),
3.62 (doublet of doublets, J=3.5, 9.6Hz, 1H),
1.28 (doublet, J=6.3Hz, 3H).

Example 34

6-methoxy-1,4a-dimethyl-7-(β -L-fucopyranosyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylic acid

A procedure similar to that described in Example 1(a) above was followed, but using L-fucose 1,2,3,4-tetraacetate and methyl 6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate to give methyl 6-methoxy 1,4a-dimethyl-7-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate as a white solid in a yield of 68%.

A procedure similar to that described in Example 1(b) above was followed, but using methyl 6-methoxy-1,4a-dimethyl-7-(2,3,4-tri-o-acetyl-β -L-fucopyranosyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate to give the titled compound as a freeze-dried product in a yield of 80%.

$[\alpha]_D$ = +64 (c=0.11, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.01 (singlet, 1H),
6.83 (singlet, 1H),

4.42 (doublet, J=9.5Hz, 1H),
3.66 (doublet, J=3.7Hz, 1H),
3.72-3.64 (multiplet, 2H),
3.62 (singlet, 3H),
3.55 (doublet of doublets, J=3.7, 9.5Hz, 1H),
2.65 (doublet of doublets, J=4.4, 16.9Hz, 1H),
2.52 (doublet of triplets, J=5.9, 12.5Hz, 1H),
2.12 (doublet, J=12.5Hz, 1H),
2.01 (doublet of doublets, J=5.9, 13.2Hz, 1H),
1.90 (doublet, J=13.2Hz, 1H),
1.86-1.68 (multiplet, 2H),
1.42-1.33 (multiplet, 1H),
1.25 (doublet, J=11.7Hz, 1H),
1.13 (doublet of triplets, J=4.4, 13.2Hz, 1H),
1.04 (doublet, J=6.6Hz, 3H),
0.99, 0.94 (2 x singlet, 6H),
0.86 (doublet of triplets, J=4.4, 13.2Hz, 1H).

Example 35

N-(2-Hydroxy-1-hydroxymethylethyl)-2-[3-(β -L-fucopyranosyl)-4-methoxyphenyl]cetamaide

The solution of ethyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] acetate (107mg, 0.33mmol) (prepared as described in Example 5 above) and serinol (268mg, 2.93mmol) in methylene chloride was stirred at room temperature for 20 days. After removal of solvent, the residue was purified by PTLC (methylene chloride / methanol = 3 / 1) to afford 52mg of the titled product in a yield of 41%.

$[\alpha]_D^{20}$ = -11 (c=0.99 methanol)

Nuclear Magnetic Resonance Spectrum (270MHz, CD_3CD) δ ppm:
7.37 (1H, doublet, J=2.1Hz),
7.11 (1H, doublet of doublets, J=2.1, 8.5Hz),

6.83 (1H, doublet, J=8.5Hz),
3.73-3.86 (3H, multiplet),
3.71 (3H, singlet),
3.63 (1H, doublet, J=1.9Hz),
3.45-3.56 (1H, multiplet),
3.42 (2H, singlet),
3.20-3.25 (4H, multiplet),
1.14 (3H, doublet, J=6.4Hz).

Example 36

[2'-Methoxy-3'-(β-L-fucopyranosyl)biphenyl-4-yl]acetic acid

Example 36(a)

Methyl (2'-methoxybiphenyl-4-yl)acetate

A solution of 2-methoxyphenylboronic acid (1.52g 10.0mmol), methyl 4-bromophenylacetate (2.14g, 10.0mmol), tetrakis(triphenylphosphine)palladium(o) (350mg, 0.30mmol) and a 2M sodium carbonate aqueous solution (5ml, 10 mmol) in toluene (40ml) was refluxed for 6 hours under a nitrogen atmosphere. The mixture was filtered-off through a celite pad and washed with water (30ml). The organic material was extracted with chloroform. The combined organic extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure. A purification by column chromatography on silica gel with ethyl acetate/hexane (10/1) afforded 1.68g of the titled product in a yield of 68.8%.

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.49 (doublet, J=8.6Hz, 2H),
7.29-7.34 (multiplet, 4H),
7.02 (triplet, J=6.6Hz, 1H),
6.98 (doublet, J=8.6Hz, 1H),
3.81 (singlet, 3H),
3.71 (singlet, 3H),
3.67 (singlet, 2H).

Example 36(b)

Methyl [2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-4-yl]acetate

To a solution of L-fucose 1,2,3,4-tetraacetate(502mg, 1.5mmol) and methyl (2'-methoxybiphenyl-4-yl)acetate (prepared as described in Example 36(a) above) (712mg, 2.9mmol) and silver triflucroacetate (500mg, 2.3mmol) in methylene chloride

(5ml) at 0°C was added a 1M methylene chloride solution of tin(IV) chloride (2.3ml, 2.3mmol) under a nitrogen gas atmosphere. After the reaction mixture was stirred for 4 hours at 0°C and for 12 hours at room temperature, a saturated aqueous solution of sodium bicarbonate was added and stirred for 20 minutes. The insoluble material was filtered-off through a celite pad and the filtrate was extracted with methylene chloride several times. The combined methylene chloride solution was washed with brine and dried over anhydrous magnesium sulfate, then concentrated under reduced pressure. A purification by column chromatography with hexane/ethyl acetate (3/1) afforded 501mg of the titled product in a yield of 54.5%.

$[\alpha]_D^{20}$ = +25.7 (c=1.24, methylene chloride)

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.47 (doublet, J=7.9Hz, 2H),
7.35-7.26 (multiplet, 4H),
6.93 (doublet, J=7.9Hz, 1H),
5.40 (triplet, J=9.9Hz, 1H),
5.36 (triplet, J=3.3Hz, 1H),
5.18 (doublet of doublets, J=3.3, 9.9Hz, 1H),
4.32 (doublet, J=9.9Hz, 1H),
3.95 (quartet, J=5.9Hz, 1H),
3.79 (singlet, 3H),
3.72 (singlet, 3H),
3.67 (singlet, 2H),
2.23 (singlet, 3H),
1.99 (singlet, 3H),
1.81 (singlet, 3H),
1.22 (doublet, J=5.9Hz, 3H).

Example 36(c)

[2'-Methoxy-3'-(β-L-fucopyranosyl)biphenyl-4-yl]acetic acid

A procedure similar to that described in Example 1(b) above was followed, but using methyl [2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-4-yl]acetate (prepared as described in Example 36(b) above) to give the titled compound as a freeze-dried product in a yield of 82%.

$[\alpha]_D$ = -10.0 (c=0.43, methanol)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.41 (doublet, J=4.4Hz, 2H),
7.36-7.40 (multiplet, 2H),
7.32 (doublet, J=8.3Hz, 2H),
7.02 (doublet, J=8.3Hz, 1H),
4.04 (doublet, J=9.7Hz, 1H),
3.74 (quartet, J=6.4Hz, 1H),
3.71-3.63 (multiplet, 2H),
3.64 (singlet, 3H),
3.57 (doublet of doublets, J=3.4, 9.7Hz, 1H),
3.38 (singlet, 2H),
1.06 (doublet, J=6.4Hz, 3H).

Example 37

[2'-Methoxy-3'-(β-L-fucopyranosyl)biphenyl-3-yl]acetic acid

Example 37(a)

Methyl (2'-methoxybiphenyl-3-yl)acetate

A procedure similar to that described in Example 36(a) above was followed, but using 2-methoxyphenylboronic acid and methyl 3-bromophenylacetate to give the titled compound as an oil in a yield of 80.1%.

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.47-7.24 (multiplet, 6H),
7.03 (triplet, J=7.9Hz, 1H),

6.98 (triplet, J=7.9Hz, 1H),
3.81 (singlet, 3H),
3.70 (singlet, 3H),
3.68 (singlet, 2H).

Example 37(b)

Methyl[2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-3-yl]acetate

A procedure similar to that described in Example 36(b) above was followed, but using methyl (2'-methoxybiphenyl-3-yl)acetate (prepared as described in Example 37(a) above) to give the titled compound as a white solid in a yield of 47.0%.

$[\alpha]_D^{23}$ = +21 (c=0.62, methylene chloride)

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.41-7.25 (multiplet, 6H,),
6.94 (triplet, J=8.6Hz, 1H),
5.41 (triplet, J=9.9Hz, 1H),
5.33 (doublet, J=3.3Hz, 1H),
5.18 (doublet of doublets, J=9.9, 3.3Hz, 1H),
4.33 (doublet, J=9.9Hz, 1H),
3.96 (quartet, J=6.6Hz, 1H),
3.79 (singlet, 3H),
3.70 (singlet, 3H),
3.68 (singlet, 2H),
2.23 (singlet, 3H),
1.99 (singlet, 3H),
1.83 (singlet, 3H),
1.23 (doublet, J=6.6Hz, 3H).

Example 37(c)

[2'-Methoxy-3'-(β-L-fucopyranosyl)biphenyl-3-yl]acetic acid

A procedure similar to that described in Example 1 (b) above was followed, but using methyl [2'-methoxy-3'-(2,3,4-tri-

O-acetyl-β-L-fucopyranosyl)biphenyl-3-yl]acetate (prepared as described in Example 37(b) above) to give the titled compound as a freeze-dried product in a yield of 85%.

[α] = -9.3 (c=0.56, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.22-7.27 (multiplet, 5H),
7.10-7.08 (multiplet, 1H),
6.98 (doublet, J=7.8Hz, 1H),
4.01 (doublet, J=9.3Hz, 1H),
3.72 (quartet, J=6.3Hz, 1H),
3.70 (doublet, J=3.4Hz, 1H),
3.65 (triplet, J=9.3Hz, 1H),
3.63 (singlet, 3H),
3.56 (doublet of doublets, J=3.4, 9.3, 1H),
3.37 (singlet, 2H),
1.05 (doublet, J=6.3Hz, 3H).

Example 38

[2'-Methoxy-3'-β-L-fucopyranosyl)biphenyl-2-yl]acetic acid

Example 38(a)

Methyl (2'-methoxybiphenyl-2-yl)acetate

A procedure similar to that described in Example 36(a) above was followed, but using 2-methoxyphenylboronic acid and methyl 2-bromophenylacetate to give the titled compound as an oil in a yield of 63.8%.

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.35-7.14 (multiplet, 6H),
7.01 (triplet, J=7.2Hz, 1H),
6.95 (doublet, J=8.6Hz, 1H),
3.72 (singlet, 3H),
3.57 (singlet, 3H),
3.50 (singlet, 2H).

Example 38(b)

Methyl [2'-methoxy-3' and 5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-2-yl]acetate (1:1 mixture)

A procedure similar to that described in Example 36(b) above was followed, but using methyl (2'-methoxybiphenyl-2-yl)acetate (prepared as described in Example 38(a) above) to give the titled compound as a white solid in a yield of 22%. Two products could not be separated by column chromatography.

$[\alpha]_D^{23}$ + 23 (c = 0.70, methylene chloride)

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.41-7.15 (multiplet, 6H),
6.90 (doublet of doublets, J=8.6, 3.3Hz, 1H),
5.36 (triplet, J=9.9Hz, 1H),
5.35 (doublet, J=3.3Hz, 1H),
5.16 (doublet of doublets, J=9.9, 3.3Hz, 1H),
4.30 (doublet, J=9.9Hz, 1H),
3.94 (quartet, J=6.6Hz, 1H),
3.71 (singlet, 3H,),
3.62 (singlet, 1.5H),
3.59 (singlet, 1.5H),
3.46 (singlet, 2H),
2.22 (singlet, 3H),
1.99 (singlet, 3H),
1.86 (singlet, 1.5H),
1.81 (singlet, 1.5H),
1.21 (doublet, J=6.6Hz, 3H).

Example 38(c)

(2'-Methoxy-3'-β-L-fucopyranosyl)biphenyl-2-yl]acetic acid

A procedure similar to that described in Example 1(b) above was followed, but using methyl [2'-methoxy-3' and 5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-2-yl]acetate

(prepared as described in Example 38(b) above) to give the titled compound as a freeze-dried product in a yield of 80%.

$[\alpha]_D$ = -5.8 (c=0.83, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.31-7.14 (multiplet, 4H),
7.04-6.92 (multiplet, 3H),
4.59 (broad singlet, 1H),
3.99 (doublet of doublets, J=5.1, 9.5Hz, 1H),
3.74-3.53 (multiplet, 3H),
3.56 (singlet, 3H),
3.17-3.07 (multiplet, 2H),
1.05 (doublet, J=6.8Hz, 3H).

Example 39

2'-Methoxy-3'-(β-L-fucopyranosyl)biphenyl-4-carboxylic acid

Example 39(a)

Methyl 4-(2'-methoxyphenyl)benzoate

A procedure similar to that described in Example 36(a) above was followed, but using 2-methoxyphenylboronic acid and methyl 4-bromobenzoate to give the titled compound as an oil in a yield of 28.7%.

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.87 (doublet, J=6.6, 1H),
7.55 (triplet, J=7.3Hz, 1H),
7.42-7.24 (multiplet, 4H),
7.04 (triplet, J=7.3Hz, 1H),
6.91 (doublet, J=8.6Hz, 1H),
3.72 (singlet, 3H),
3.66 (singlet, 3H).

Example 39(b)

Methyl 2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-4-carboxylate

A procedure similar to that described in Example 36(b) above was followed, but using methyl 4-(2'-methoxyphenyl) benzoate (prepared as described in Example 39(a) above) to give the titled compound as a foam in a yield of 31.6%.

$[\alpha]_D^{23}$ = -10 (c=0.32, methylene chloride)

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.88 (doublet, J=7.9Hz, 1H),
7.56 (triplet, J=7.9Hz, 1H),
7.43 (doublet, J=7.9Hz, 1H),
7.40 (doublet, J=7.9Hz, 1H),
7.32 (doublet, J=7.9Hz, 1H),
7.23 (singlet, 1H),
6.87 (doublet, J=7.9Hz, 1H),
5.37 (doublet, J=3.3Hz, 1H),
5.36 (triplet, J=9.9Hz, 1H),
5.18 (doublet of doublets, J=9.9, 3.3Hz, 1H),
4.33 (doublet, J=9.9Hz, 1H),
3.97 (doublet, J=7.3Hz, 1H),
3.70 (singlet, 3H),
3.61 (singlet, 3H),
2.23 (singlet, 3H),
2.05 (singlet, 3H),
1.99 (singlet, 3H),
1.28 (doublet, J=7.3Hz, 3H).

Example 39(c)

2'-Methoxy-3'-(β-L-fucopyranosyl)biphenyl-4-carboxylic acid

A procedure similar to that described in Example 1(b) above was followed, but using methyl 2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-4-carboxylate (prepared as

described in Example 39(b) above) to give the titled compound as a freeze-dried product in a yield of 78%.

$[\alpha]_D$ = -2.1 (c=0.33, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.39-7.13 (multiplet, 6H),
6.87 (doublet, J=8.3Hz, 1H),
4.01 (doublet, J=9.8Hz, 1H),
3.74 (quartet, J=6.4Hz, 1H),
3.68 (doublet of doublets, J=1.0, 3.4Hz, 1H),
3.66 (triplet, J=9.8Hz, 1H),
3.57 (doublet of doublets, J=3.4, 9.8Hz, 1H),
3.55 (singlet, 3H),
1.06 (doublet, J=6.4Hz, 3H).

Example 40

2-[3'-(β-L-Fucopyranosyl)-2'-methoxybiphenyl-4-yl]ethanol

To a solution of methyl [2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-4-yl]acetate (prepared as described in Example 36(b) above) (163mg, 0.26mmol) in tetrahydrofuran was added lithium aluminum hydride (30mg, 0.79mmol) portion wise at -78°C. The mixture was gradually warmed up to room temperature over 3 hours. Then, additional lithium aluminum hydride (15mg, 0.40mmol) was added. After 18 hours, a sodium hydroxide aqueous solution was added. The mixture was stirred vigorously for 15 minutes. The insoluble material was filtered off through a celite pad. The filtrate was evaporated under reduced pressure. A purification by PTLC with ethyl acetate / methanol / water (20 / 4 / 1) afforded 41mg of the titled compound in a yield of 41.4%.

$[\alpha]_D^{23}$ = -8.8 (c = 0.17, methanol)

Nuclear Magnetic Resonance Spectrum (270MHz, CD_3OD) δ ppm:

7.16-7.31 (multiplet, 6H),
6.98 (doublet, J=8.8Hz, 1H),

4.00 (doublet, J=9.8Hz, 1H),
3.65-3.74 (multiplet, 6H),
3.63 (singlet, 3H),
3.56 (doublet of doublets, J=3.4, 9.8Hz, 1H),
2.71 (triplet, J=6.6Hz, 2H),
1.05 (doublet, J=6.4Hz, 3H).

Example 41

2-[3'-(β-L-Fucopyranosyl)-2'-methoxybiphenyl-3-yl]ethanol

A procedure similar to that described in Example 40 above was followed, but using methyl [2'-methoxy-3'-(2,3,4-tri-O acetyl-β-L-fucopyranosyl)biphenyl-3-yl]acetate (prepared as described in Example 37(b) above) to give the titled compound as an oil in a yield of 36.6%.

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.39-7.26 (multiplet, 5H),
7.13 (doublet, J=7.3Hz, 1H),
7.00 (doublet, J=8.2Hz, 1H),
4.02 (doublet, J=9.3Hz, 1H),
3.77-3.52 (multiplet, 3H),
3.75 (singlet, 3H),
3.32-3.27 (multiplet, 3H),
2.82 (triplet, J=7.1Hz, 2H),
1.25 (doublet, J=6.5Hz, 3H).

Example 42

2-[3'-(β-L-Fucopyranosyl-2'-methoxybiphenyl-2-yl]ethanol

A procedure similar to that described in Example 40 above was followed, but using methyl [2'-methoxy-3' and 5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-2-yl]acetate (prepared as described in Example 38(b) above) to give the titled compound as an oil in a yield of 50.0%.

Nuclear Magnetic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.35 (doublet, J=9.5Hz, 1H),

7.21-7.07 (multiplet, 4H),
7.00 (doublet, J=7.1Hz, 1H),
6.93 (doublet, J=8.5Hz, 1H),
3.94 (doublet, J=9.4Hz, 1H),
3.66-3.55 (multiplet, 1H),
3.63 (singlet, 3H),
3.40-3.50 (multiplet, 3H),
3.25-3.20 (multiplet, 2H),
2.62-1.58 (multiplet, 2H),
1.17 (doublet, J=6.4Hz, 3H).

Example 43

2-[3-(β-L-Fucopyranosyl)-4-methoxyphenyl]ethanol

A procedure similar to that described in Example 40 above was followed, but using ethyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]acetate (prepared as described in the first half of Example 5 above) to give the titled compound as an oil in a yield of 57%.

$[\alpha]_D$ = -13 (c=0.33, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.19 (doublet, J=2.0Hz, 1H),
7.08 (doublet of doublets, J=2.0, 8.3Hz, 1H),
6.85 (doublet, J=8.3Hz, 1H),
4.51 (doublet, J=9.8Hz, 1H),
3.75-3.55 (multiplet, 6H),
3.63 (singlet, 3H),
2.62 (triplet, J=6.6Hz, 2H),
1.04 (doublet, J=6.4Hz, 3H).

Example 44

2-[3-(α-L-Fucopyranosyl)-4-methoxyphenyl]ethanol

A procedure similar to that described in Example 40 above was followed, but using ethyl [4-methoxy-3-(2,3,4-tri-O-acetyl-

α-L-fucopyranosyl)phenyl]acetate (prepared as described in the first half of Example 6 above) to give the titled compound as an oil in a yield of 80%.

$[\alpha]_D$ = -0.8 (c=0.52, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.16 (doublet, J=2.2Hz, 1H),
7.07 (doublet of doublets, J=2.2, 8.6Hz, 1H),
6.85 (doublet, J=8.6Hz, 1H),
5.29 (doublet, J=3.4Hz, 1H),
4.01-3.90 (multiplet, 2H),
3.89-3.87 (multiplet, 2H),
3.66 (singlet, 3H),
3.62 (triplet, J=6.6Hz, 2H),
2.63 (triplet, J=6.6Hz, 2H),
1.15 (doublet, J=6.8Hz, 3H).

Example 45

[5-(β-L-Fucopyranosyl)-6-methoxynaphthalene-1-yl]methanol

A procedure similar to that described in Example 40 above was followed, but using methyl 6-methoxy-5-(2,3,4-tri-o-acetyl-β-L-fucopyranosyl)naphthalene-1-carboxylate (prepared as described in the first half of Example 32 above) to give the titled compound as a white solid in a yield of 54%.

$[\alpha]_D$ = -4.5 (c=0.29, methanol)

Nuclear Magnetic Resonance Spectrum (270MHz, CD_3OD) δ ppm:
8.84-8.80 (multiplet, 1H),
8.19 (doublet, J=9.4Hz, 1H),
7.47-7.40 (multiplet, 3H),
5.35 (doublet, J=9.6Hz, 1H),
5.07 (singlet, 2H),
4.43 (triplet, J=9.6Hz, 1H),
3.99 (singlet, 3H),
3.87 (doublet, J=3.2Hz, 1H),

3.83 (quartet, J=6.5Hz, 1H),
3.68 (doublet of doublets, J=3.2, 9.6Hz, 1H),
1.35 (doublet, J=6.5Hz, 3H).

Example 46

Sodium 2-[3'-(sodium β-fucopyranosyl-2,3,4-trisulfate)-2'-methoxybiphenyl-4-yl]ethyl sulfate

To a solution of 2-[3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-4-yl]ethanol (prepared as described in Example 40 above) (78mg, 0.21mmol) in dimethylformamide (5ml) was added pyridinium sulfur trioxide (400mg, 2.5mmol) at room temperature under a nitrogen atmosphere. After 2 hours, i-propylether (20ml) was added. Then a white precipitate was appeared. The organic solvent was decanted and the resultant residue was purified by using IATROBEADS™ column chromatography (methylene chloride methanol / water / pyridine = 70 / 25 / 3 / 3). Fractions containing pure compound were evaporated and dried under high vacuum. The product was converted into a sodium salt by passing it through Dowex-50-X-8 (Na+) resin in water and subjecting it to lyophilization that afforded 118mg of a freeze-dried product in a yield of 72.1%.

$[\alpha]_D^{20}$ = -0.9 (c=0.33, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.33 (doublet, J=8.3Hz, 2H),
7.27 (doublet of doublets, J=2.2, 8.8Hz, 1H),
7.22 (doublet, J=2.2Hz, 1H),
7.20 (doublet, J=8.3Hz, 2H),
6.93 (doublet, J=8.8Hz, 1H),
4.84 (doublet, J=2.5Hz, 1H)
4.49 (triplet, J=9.3Hz, 1H),
4.43 (doublet of doublets, J=2.5, 9.3Hz, 1H),
4.29 (doublet, J=9.3Hz, 1H),
4.12 (triplet, J=6.8Hz, 2H),

3.89 (quartet, J=6.4Hz, 1H),
3.62 (singlet, 3H),
2.87 (triplet, J=6.8Hz, 2H),
1.12 (doublet, J=6.4Hz, 3H).

Example 47

Sodium 2-[3'-(sodium β-L-fucopyranosyl-2 3,4-trisulfate)-2'-methoxybiphenyl-3-yl]ethyl sulfate

A procedure similar to that described in Example 46 above was followed, but using 2-[3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-3-yl]ethanol (prepared as described in Example 41, above) to give the titled compound as a freeze-dried product in a yield of 26.4%.

$[\alpha]_D^{20}$ = -1.2 (c=0.26, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.14-7.34 (multiplet, 6H),
7.02 (doublet, J=8.3Hz, 1H),
4.77 (doublet, J=2.4Hz, 1H),
4.41 (triplet, J=9.8Hz, 1H),
4.35 (doublet of doublets, J=2.4, 9.8Hz, 1H),
4.21 (doublet, J=9.8Hz, 1H),
4.13 (triplet, J=6.8Hz, 2H),
3.88 (quartet, J=6.3Hz, 1H),
3.66 (singlet, 3H),
2.89 (triplet, J=6.8Hz, 2H),
1.13 (doublet, J=6.3Hz, 3H).

Example 48

1,4-Dimethoxy-2-(sodium β-L-fucopyranosyl-2,3,4-trisulfate)benzene

A procedure similar to that described in Example 46 above was followed, but using 1,4-dimethoxy-2-(β-L-fucopyranosyl) benzene (prepared from 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-

fucopyranosyl)benzene as described in Example 31 above, but using L-fucose 1,2,3,4-tetraacetate and 1,4-dimethylbenzene) to give the titled compound as a white solid in a yield of 39%.

$[\alpha]_D$ = -3.5 (c=0.31, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
6.92 (broad singlet, 1H),
6.82 (doublet, J=9.3Hz, 1H),
6.75 (doublet, J=9.3Hz, 1H),
4.85 (doublet, J=2.4Hz, 1H),
4.82-4.45 (multiplet, 2H),
4.42 (doublet, J=8.6Hz, 1H),
3.91-3.85 (multiplet, 1H),
3.63, 3.63 (2 x singlet, 6H),
1.12 (doublet, J=6.4Hz, 3H).

Example 49

1,4-Dimethoxy-2-(sodium β-D-galactopyranosyl-2,3,4,6-tetrasulfate)benzene

A procedure similar to that described in Example 46 above was followed, but using 1,4-dimethoxy-2-(β-D-galactopyranosyl) benzene (prepared as described in Example 31 above) to give the titled compound as a freeze-dried compound in a yield of 82%.

$[\alpha]_D$ = +1.9 (c=0.37, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
6.93 (broad singlet, 1H),
6.82 (doublet, J=9.3Hz, 1H),
6.77 (doublet of doublets, J=2.9, 9.3Hz, 1H),
5.00 (doublet, J=2.5Hz, 1H),
4.70-4.55 (broad singlet, 2H),
4.45 (doublet of doublets, J=2.5, 9.3Hz, 1H),
3.98-4.11 (multiplet, 3H),
3.64, 3.63 (2 x singlet, 6H).

Example 50

2,6-Dimethoxy-1-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)naphthalene

A procedure similar to that described in Example 46 above was followed, but using 2,6-dimethoxy-1-(β-L-fucopyranosyl) naphtalene (prepared using L-fucose 1,2,3,4-tetraacetate and 2,6-dimethoxynaphthalene as described in Example 31 above) to give the titled compound as a freeze-dried product in a yield of 39%.

$[\alpha]_D$ = -31 (c=0.25, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
8.66 (doublet, J=9.3Hz, 1H),
8.36 (doublet, J=9.3Hz, 1H),
7.21-7.12 (multiplet, 3H),
5.37 (doublet, J=9.8Hz, 1H),
5.00 (triplet, J=9.8Hz, 1H),
4.97 (doublet, J=2.7Hz, 1H),
4.50 (doublet of doublets, J=2.7, 9.8Hz, 1H),
3.96 (quartet, J=6.4Hz, 1H),
3.77, 3.75 (2 x singlet, 6H),
1.18 (doublet, J=6.4Hz, 3H).

Example 51

2,6-Dimethoxy-1-(sodium 3-β-galactopyranosyl 2,3,4,6-tetrasulfate)naphthalene

A procedure similar to that described in Example 46 above was followed, but using 2,6-dimethoxy-1-(β-D-galactophyranosyl) naphthalene (prepared using β-D-galactose 1,2,3,4,6-pentaacetate and 2,6-dimethoxynaphthalene as described in Example 31 above) to give the titled compound as a freeze-dried product in a yield of 74%.

$[\alpha]_D$ = +4.5 (c=0.25, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

8.34 (doublet, J=8.8Hz, 1H),
7.66 (doublet, J=8.8Hz, 1H),
7.19 (doublet, J=8.8Hz, 1H),
7.14 (doublet, J=2.2Hz, 1H),
7.12 (doublet of doublets, J=2.2, 8.8Hz, 1H),
5.40 (doublet, J=9.5Hz, 1H),
5.11 (doublet, J=2.2Hz, 1H),
5.00 (triplet, J=9.5Hz, 1H),
4.53 (doublet of doublets, J=2.2, 9.5Hz, 1H),
4.19-4.03 (multiplet, 3H),
3.76, 3.74 (2 x singlet, 6H).

Example 52

Sodium[4-methoxy-3-(sodium-β-L-fucopyranosyl 2,3,4-trisulfate)acetate

A procedure similar to that described in Example 61 below was followed, but using ethyl [4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]acetate (prepared as described in the first half of Example 5 above) to give the titled compound as a freeze-dried product in a yield of 42%.

$[\alpha]_D$ = +1.6 (c=0.32, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.07-7.02 (multiplet, 2H),
6.79 (doublet, J=8.8Hz, 1H),
4.83 (doublet, J=2.4Hz, 1H),
4.58-4.68 (multiplet, 2H),
4.40 (doublet, J=8.8Hz, 1H),
3.84-3.88 (broad doublet, J=6.4Hz, 1H),
3.66 (singlet, 3H),
3.28 (singlet, 2H),
1.11 (doublet, J=6.8Hz, 3H).

Example 53

Sodium 2-[4-methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]ethylsulfate

A procedure similar to that described in Example 46 above was followed, but using 2-[3-(β-L-fucopyranosyl)-4-methoxyphenyl]ethanol (prepared as described in Example 43 above) to give the titled compound as a freeze-dried product in a yield of 42%.

$[\alpha]_D$ = -8.3 (c=0.35, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.22 (doublet, J=2.4Hz, 1H),
7.14 (doublet of doublets, J=2.4, 8.3Hz, 1H),
6.86 (doublet, J=8.3Hz, 1H),
4.75 (doublet, J=2.9Hz, 1H),
4.62 (doublet, J=9.8Hz, 1H),
4.32 (doublet of doublets, J=2.9, 9.8Hz, 1H),
4.07-4.02 (multiplet, 3H),
3.87 (quartet, J=6.4Hz, 1H),
3.65 (singlet, 3H),
2.79 (triplet, J=6.8Hz, 2H),
1.09 (doublet, J=6.4Hz, 3H).

Example 54

Sodium [6-methoxy- 5-(sodium β-L-fucopyranosyl 2,4-disulfate)naphthalene-1-yl]methylsulfate

A procedure similar to that described in Example 46 above was followed, but using [5-(β-L-fucopyranosyl)-6-methoxynaphthalene-1-yl]methanol (prepared as described in Example 45 above) to give the titled compound as a freeze-dried product in a yield of 59%.

$[\alpha]_D$ = -14 (c=0.24, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
8.46 (doublet, J=8.8Hz, 1H),

8.03 (doublet, J=9.3Hz, 1H),
7.43-7.32 (multiplet, 3H),
5.41 (doublet, J=11.2Hz, 1H),
5.34 (doublet, J=9.5Hz, 1H),
5.24 (doublet, J=11.2Hz, 1H),
4.93 (triplet, J=9.5Hz, 1H,
4.63 (doublet, J=2.9Hz, 1H),
3.98-3-91 (multiplet, 2H),
3.80 (singlet, 3H),
1.17 (doublet, J=6.4Hz, 3H).

Example 55

Sodium [6-methoxy-5-sodium β-L-fucopyranosyl 2,3,4-trisulfate)naphthalene-1-yl]methylsulfate

A procedure similar to that described in Example 46 above was followed, but using [5-(β-L-fucopyranosyl)-6-methoxynaphthalene-1-yl]methanol (prepared as described in Example 45 above) to give the titled compound as a freeze-dried product in a yield of 76%.

$[\alpha]_D$ = -19 (c=0.18, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
8.49 (doublet, J=8.8Hz, 1H),
8.02 (doublet, J=9.8Hz, 1H),
7.43-7.32 (multiplet, 3H),
5.44 (doublet, J=9.8Hz, 1H),
5.42 (doublet, J=10.7Hz, 1H),
5.23 (doublet, J=10.7Hz, 1H),
5.03 (triplet, J=9.8Hz, 1H),
4.97 (doublet, J=2.9Hz, 1H),
4.50 (doublet of doublets, J=2.9, 9.8Hz, 1H),
3.97 (quartet, J=6.3Hz, 1H),
3.81 (singlet, 3H),
1.18 (doublet, J=6.3Hz, 3H).

Example 56

Sodium 1-[4-methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]cyclohexanecarboxylate

A procedure similar to that described in Example 61 below was followed, but using methyl 1-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexane carboxylate (prepared as described in the first half of Example 7 above) to give the titled compound as a freeze-dried product in a yield of 89%.

$[\alpha]_D$ = -9.1 (c=1.32, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
7.22 (singlet, 1H),
7.15 (doublet, J=8.8Hz, 1H),
6.77 (doublet, J=8.8Hz, 1H),
4.52 (doublet, J=2.9Hz, 1H),
4.41 (doublet, J=9.5Hz, 1H),
4.31 (doublet of doublets, J=2.9, 9.5Hz, 1H),
4.08 (triplet, J=9.5Hz, 1H),
3.83 (quartet, J=6.6Hz, 1H),
3.64 (singlet, 3H),
2.03-2.00 (multiplet, 2H),
1.10 (doublet, J=6.6Hz, 3H),
1.50-1.06 (multiplet, 8H).

Example 57

Sodium 2-[4-methoxy-3-(sodium α-L-fucopyranosyl 2,3,4-trisulfate)phenyl]ethylsulfate

A procedure similar to that described in Example 46 above was followed, but using 2-[3-(α-L-fucopyranosyl)-4-methoxyphenyl]ethanol (prepared as described Example 44 above) to give the titled compound as a freeze-dried product in a yield of >99%.

$[\alpha]_D$ = +2.0 (c=0.66, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:

7.13 (doublet, J=2.4Hz, 1H),
7.07 (doublet of doublets, J=2.4, 8.3Hz, 1H),
6.79 (doublet, J=8.3Hz, 1H),
5.38 (singlet, 1H),
4.94 (triplet, J=3.7Hz, 1H),
4.85 (doublet, J=3.7Hz, 1H),
4.70 (doublet of doublets, J=3.7, 6.8Hz, 1H),
4.39 (quartet, J=6.8Hz, 1H),
4.03 (triplet, J=7.3Hz, 2H),
3.65 (singlet, 3H),
2.79 (triplet, J=7.3Hz, 2H),
1.30 (doublet, J=6.8Hz, 3H).

Example 58

Sodium-2-[3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-4-yl]ethylsulfate

To a solution of 2-(3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-4-yl]ethanol (prepared as described in Example 40 above) (153mg, 0.25mmol) in pyridine (5ml) was added pyridinium sulfur trioxide (400mg, 2.5mmol) at room temperature under a nitrogen atmosphere. The mixture was stirred for 18 hours. After being quenched by an addition of methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (methylene chloride / methanol / water / pyridine = 80 / 20 / 2 / 1). Fractions containing pure compound were evaporated and dried under high vacuum. The product was converted into a sodium salt by passing it through Dowex-50-X-8 (Na+) resin in water and was subjected to lyophilization that afforded 15mg of a freeze-dried product in a yield of 35.6%.

$[\alpha]_D^{20}$ = +6.4 (c=0.11, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.35-7.22 (multiplet, 6H),
7.00 (doublet, J=8.3Hz, 1H),
4.15 (triplet, J=6.8Hz, 2H),
4.03 (doublet, J=9.8Hz, 1H),
3.74 (quartet, J=6.8Hz, 1H),
3.69 (doublet, J=3.4Hz, 1H),
3.65 (singlet, 3H),
3.67-3.64 (multiplet, 1H),
3.58 (doublet of doublets, J=9.8, 3.4Hz, 1H),
2.87 (triplet, J=6.8Hz, 2H),
1.07 (doublet, J=6.4Hz, 3H).

Example 59

Sodium 2-[3'-β-L-(fucopyranosyl)-2'-methoxybiphenyl-3-yl]ethylsulfate

A procedure similar to that described in Example 58 above was followed, but using 2-[3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-3-yl]ethanol (prepared as described in Example 41 above) to give the titled compound as a freeze-dried product in a yield of 5.6%.

$[\alpha]_D^{20}$ = -5.9 (c=0.22, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.23-7.30 (multiplet, 5H),
7.14-7.17 (multiplet, 1H),
6.99 (doublet, J=8.3Hz, 1H),
4.12 (triplet, J=6.4Hz, 2H),
4.02 (doublet, J=9.3Hz, 1H),
3.74 (quartet, J=6.4Hz, 1H),
3.68 (doublet, J=3.4Hz, 1H),
3.66 (triplet, J=9.3Hz, 1H),
3.64 (singlet, 3H),
3.57 (doublet of doublets, J=3.4, 9.3Hz, 1H),

2.88 (triplet, J=6.4Hz, 2H),
1.06 (doublet, J=6.4Hz, 3H).

Example 60

Sodium 2-[3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-2-yl] ethylsulfate

A procedure similar to that described in Example 58 above was followed, but using 2-[3'-(β-L-fucopyranosyl)-2'-methoxybiphenyl-2-yl]ethanol (prepared as described in Example 42 above) to give the titled compound as a freeze-dried product in a yield of 39.3%.

$[\alpha]_D^{20}$ = -5 (c=0.2, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.37-6.96 (multiplet, 7H),
4.00 (doublet of doublets, J=9.3, 2.0Hz, 1H),
3.86-3.80 (multiplet, 2H),
3.73 (quartet, J=6.4Hz, 1H),
3.59 (singlet, 3H),
3.67-3.53 (multiplet, 3H),
2.67-2.60 (multiplet, 2H),
1.05 (doublet, J=6.4Hz, 3H).

Example 61

Sodium [2'-methoxy-3'-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)biphenyl-4-yl]acetate

To a solution of methyl [2'-methoxy-3'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-4-yl]acetate prepared as described in Example 36(b) above) (153mg, 0.25mmol) in methanol was added sodium methoxide methanol solution dropwise at room temperature. The mixture was stirred for 6 hours and AMBERLITE® was added to neutralize the solution. The inorganic materials were filtered-off and the filtrate was evaporated under reduced pressure. The residue was purified by using PTLC (ethyl acetate

/ methanol = 20 / 1) and was extracted with methanol. Solvent was removed under reduced pressure, then the resultant residue was dissolved in dimethylformamide (5ml) and pyridinium sulfur trioxide (360mg, 2.3mmol) was added. The mixture was stirred at room temperature for 2 days. After being quenched by an addition of methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (methylene chloride / methanol / water / pyridine = 140 / 60 / 2 / 1). Fractions containing pure compound were evaporated and dried under high vacuum, and then dissolved with water. To the solution was added sodium hydroxide (400mg) at room temperature. After 2 hours, AMBERLITE® was added at 0°C and inorganic materials were filtered-off through a celite pad. The filtrate was evaporated and the residue was purified by using IATROBEADS™ column chromatography (methylene chloride / methanol / water / pyridine = 70 / 30 / 5 / 5). Fractions containing pure compound were evaporated and dried under high vacuum. The product was converted into a sodium salt by passing it through Dowex-50-X-8 (Na+) resin in water and subjected to lyophilization that afforded 65mg of a freeze-dried product in a yield of 37.6%.

$[\alpha]_D^{23}$ = +5.8 (c=0.31, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.27-7.33 (multiplet, 3H),
7.23 (doublet, J=2.4Hz, 1H),
7.15 (doublet, J=8.3Hz, 2H),
6.95 (doublet, J=8.3Hz, 1H),
4.85 (doublet, J=2.4Hz, 1H),
4.50 (triplet, J=9.3Hz, 1H),
4.44 (doublet of doublets, J=2.4, 9.3Hz, 1H),
4.30 (doublet, J=9.3Hz, 1H),
3.90 (quartet, J=6.4Hz, 1H),
3.63 (singlet, 3H),

3.39 (singlet, 2H),
1.13 (doublet, J=6.4Hz, 3H).

Example 62
6-(β-L-Fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)benzene

Example 62(a)
1,3-Dimethoxy-4-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosonate)benzene

Under an argon gas atmosphere, a 1M methylene chloride solution (9ml, 9mM) of tin(IV) chloride was added to a reaction mixture of 1,3-dimethoxybenzene (828mg, 6mM), methyl 5-acetamido-2,4,7,8,9-penta-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosonate (1.6g, 3mM), and silver trifluoroacetate (990mg, 4.5mM) in methylene chloride (40ml) at 0°C. After being stirred for 1 hour at room temperature, the reaction was quenched by adding water. The insoluble material was filtered-off through a celite pad, and the filtrate was washed by a saturated sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. A purification by column chromatography with ethyl acetate afforded 1.6g (yield 87.5%.) of the titled compound.

Example 62(b)
1,3-Dimethoxy-4-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosonate)-6-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzene

Under an argon gas atmosphere, a 1M methylene chloride solution (4ml, 4mmol) of tin(IV) chloride was added to a reaction mixture of 1,3-dimethoxy-4-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosonate)benzene (prepared as described in Example

62(a) above) (611mg, 1mmol), L-fucose 1,2,3,4-tetraacetate (664mg, 2mM), and silver trifluoroacetate (440mg, 2mmol) in methylene chloride (15ml) at 0°C. After being stirred for 8 hours at room temperature, the reaction was quenched by adding water. The insoluble material was filtered-off through a celite pad, and the filtrate was washed by saturated sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. A purification by column chromatography with ethyl acetate afforded 852mg (yield 96.4%) of the title compound.

Example 62(c)
6-(β-L-Fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)benzene

To a methanol solution (10ml) of 1,3-dimethoxy-4-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosonate)-6-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzene (prepared as described in Example 62(b) above) (852mg, 0.96mmol) was added a catalytic amount (0.1ml) of 28% sodium methoxide methanol solution. After being stirred for 2 hours, AMERLITE® G-50 was added to neutralize the reaction mixture. After filtering-off the insoluble material through a celite pad, the filtrate was evaporated under reduced pressure. The product was purified by column chromatography (ethyl acetate elution solution) afforded the ester (417mg). A reaction with 1N sodium hydroxide aqueous solution (5ml) in refluxed methanol (10ml) for 8 hours hydrolyzed the ester to acid. The resultant reaction mixture was acidified (pH 3) by adding a 1N aqueous solution of hydrogen chloride and the whole reaction mixture was concentrated under reduced pressure. A purification by column chromatography with propanol/ethanol/water (8/4/1) afforded 288mg (yield 52.1%) of the titled compound.

$[\alpha]_D$ = -58 (c=0.2, MeOH)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.50 (singlet, 1H),
6.48 (singlet, 1H),
4.41 (doublet, J=9.5Hz, 1H),
3.92 (doublet of triplets, J=4.4, 11.0Hz, 1H),
3.80 (triplet, J=9.5Hz, 1H),
3.67 (singlet, 3H),
3.63 (singlet, 3H),
3.75 - 3.61 (multiplet, 5H),
3.55 (doublet of doublets, J=2.9, 9.5Hz, 1H),
3.47 (doublet of doublets, J=2.2, 10.3Hz, 1H),
3.44 (doublet, J=5.1Hz, 1H),
3.31 (doublet, J=8.8Hz, 1H),
2.88 (doublet of doublets, J=4.4, 13.2Hz, 1H),
1.85 (singlet, 3H),
1.45 (doublet of doublets, J=11.7, 13.2Hz, 1H),
1.02 (doublet, J=6.6Hz, 3H).

Example 63

1-(β-L-Fucopyranosyl)-2,6-dimethoxy-5-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)naphthalene

A procedure similar to that described in Example 62 above was followed, but using 2,6-dimethoxy-5-(methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosonate)-1-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) naphthalene (prepared as described in Examples 62(a) and 62(b) above using 2,6-dimethoxynaphthalene instead of 1,3-dimethoxybenzene) to give the titled compound as a freeze-dried product in a yield of 84%.

$[\alpha]_D$ = -17.0 (c=0.18, water)

Nuclear Magnetic Resonance Spectrum (270MHz, CD_3OD) δ ppm:

9.28 (doublet, J=9.9Hz, 1H),

8.79 (doublet, J=9.2Hz, 1H),
7.31 (doublet, J=9.9Hz, 1H),
7.22 (doublet, J=9.2Hz, 1H),
5.23 (doublet, J=9.9Hz, 1H),
4.57-4.44 (multiplet, 1H),
4.35 (triplet, J=9.9Hz, 1H),
3.91, 3.83 (2 x singlet, 6H),
4.07-3.46 (multiplet, 9H),
2.84 (doublet of doublets, J=5.3, 13.2Hz, 1H),
2.07 (singlet, 3H),
2.10-1.95 (multiplet, 1H),
1.29 (doublet, J=6.6Hz, 3H).

Example 64

1-(β-L-Fucopyranosyl)-2,6-dimethoxy-5-(5-acetamido-3,5-dideoxy-D-glycero-β-D-galacto-2-nonulopyranosylonic acid)naphthalene

Stereoisomer of Example 63 (the compound in Example 63 is the compound where a unit of 5-acetamide-3,5 dideoxy-D-glycero-D-galacto-2-nonulopyranosylonic acid binds in the α-manner, whereas the compound in Example 64 is the compound where a unit of 5-acetamide-3,5 dideoxy-D-glycero-D-galacto-2-nonulopyranosylonic acid binds in the β-manner).

Yield: 10%

$[\alpha]_D$ = -26.9 (c=0.26, water)

Nuclear Magnetic Resonance Spectrum (270MHz, CD_3OD) δ ppm:

8.77 (doublet, J=9.9Hz, 1H),
8.57 (doublet, J=9.9Hz, 1H),
7.29 (doublet, J=9.9Hz, 1H),
7.25 (doublet, J=9.9Hz, 1H),
5.23 (doublet, J=9.9Hz, 1H),
4.36 (triplet, J=9.9Hz, 1H),
4.14 (doublet of triplets, J=4.0, 10.6Hz, 1H),
3.98, 3.89 (2 x singlet, 6H),

4.01-3.70 (multiplet, 3H),
3.68-3.34 (multiplet, 5H),
3.16 (doublet, J=8.6Hz, 1H),
2.95 (doublet, J=10.6Hz, 1H),
2.03-1.90 (multiplet, 1H),
1.89 (singlet, 3H),
1.29 (doublet, J=6.6Hz, 3H).

Example 65
2-(β-L-Fucopyranosyl)-5-(β-D-galactopyranosyl)-1,4-dimethoxybenzene

A procedure similar to that described in Example 31 above was followed, but using 2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-5-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-1,4-dimethoxybenzene (prepared using L-fucose 1,2,3,4-tetraacetate, β-D-galactose 1,2,3,4,6-pentaacetate and 1,4-dimethoxybenzene as described in Example 62 above) to give the titled compound as a freeze-dried product in a yield of 60%.
$[\alpha]_D$ = +2.3 (c=0.6, water)
Nuclear Magnetic Resonance Spectrum (270MHz, CD_3OD) δ ppm:
7.21 (singlet, 2H),
4.66 (doublet, J=9.7Hz, 1H),
4.64 (doublet, J=9.7Hz, 1H),
3.97 (doublet, J=3.3Hz, 1H),
3.82 (2 x singlet, 6H),
3.79-3.52 (multiplet, 9H),
1.25 (doublet, J=6.5Hz, 3H).

Example 66
6-(β-D-Galactopyranosyl)-1,3,5-trimethoxy-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)benzene

Example 66(a)
2-(2,3,4,6-tetra-O-acetul-β-D-galactopyranosyl)-1,3,5-trimethoxybenzene

A procedure similar to that described in Example 1(a) above was followed, but using β-D-galactose 1,2,3,4,6-pentaacetate and 1,3,5-trimethoxybenzene to give the titled compound as a foam in a yield of 71%.

Example 66(b)
6-(β-D-Galactopyranosyl)-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-1,3,5-trimethoxybenzene

To the mixture of 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-1,3,5-trimethoxybenzene (prepared as described in Example 66(a) above) (200mg, 0.401mmol), tin (II) chloride (152mg, 0.802mmol) and mercury (II) chloride (218mg, 0.802mmol) in ethylether was added 2,3,4-tri-O-benzyl-L-fucopyranosyl fluoride (263mg, 0.602mmol) at 0°C under a nitrogen atmosphere. After 1 hour, a sodium bicarbonate aqueous solution was added and insoluble materials were filtered off through a celite pad. The filtrate was extracted with methylene chloride and the combined organic layer was dried over magnesium sulfate and evaporated under reduced pressure. The residue was dissolved in methanol (8ml) and added a few drops of sodium methoxide (28% methanol solution) at room temperature. After 0.5 hour, AMBERLYST® 15 was added for neutralization and insoluble materials were filtered-off through a celite pad. The filtrate was evaporated under reduced pressure and was purified by column chromatography

(methylene chloride:methanol = 3:2) to afford the titled compound in a yield of 67.4%.

Example 67

6-(β-L-Fucopyranosyl)-2-(sodium β-galactopyranosyl-3-sulfate)-1,3,5-trimethoxybenzene

Example 67(a)

6-(3-O-p-Methoxybenzyl-β-D-galactopyranosyl)-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-1,3,5-trimethoxybenzene

The mixture of 6-(β-D-galactopyranosyl)-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-1,3,5-trimethoxybenzene (prepared as described Example 66(b) above) (3.00g, 4.02mmol) and bis (tri-n-butyltin)oxide (2.05ml, 4.02mmol) in toluene was stirred for 3 hours at 150°C, concentrated till the volume was 30ml and cooled. To the mixture were added 4-methoxybenzylchloride 1.63ml (12.1mmol) and tetra-n-butylammonium bromide (0.65g, 2.01mmol). After 4 hours at 130°C, the mixture was poured into an aqueous solution of potassium fluoride and an organic layer was extracted with ethyl acetate and dried. A purification by column chromatography (ethyl acetate) was employed to afford the titled compound in a yield of 66.0%.

Example 67(b)

6-(2,4,6-Tri-O-benzyl-3-O-p-methoxybenzyl-β-D-galactopyranosyl)-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-1,3,5-trimethoxybenzene

To the mixture of sodium hydride (55% in mineral oil) (0.40g, 9.23mmol) in dimethylformamide (10ml) was added 6-(3-O-p-methoxybenzyl-β-D-galactopyranosyl)-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-1,3,5-trimethoxybenzene [prepared as described in Example 67(a), above], (2.00g, 2.31mmol) at 0°C. After stirring for 1 hour at room temperature and 0.5 hour at 60°C,

benzylbromide (1.1ml, 9.23mmol) was added dropwise at 0°C. The mixture was stirred at room temperature for 2 hours, methanol was added and the resultant mixture was poured into water. The organic materials were extracted with methylene chloride, dried over magnesium sulfate and purified by column chromatography (hexane:ethyl acetate=4:1) to afford the titled compound in a yield of 76.2%.

Example 67(c)

2-(2,3,4-Tri-O-benzyl-β-L-fucopyranosyl)-6-(2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-1,3,5-trimethoxybenzene

To 6-(2,4,6-tri-O-benzyl-3-O-p-methoxybenzyl-β-D-galactopyranosyl)-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-1,3,5-trimethoxybenzene (prepared as described in Example 67(b) above) (1.87g, 1.64mmol) in methylene chloride (38ml) and water (2ml) was added 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) (0.56g, 2.47mmol) at room temperature. After 1 hour, a sodium bicarbonate aqueous solution was added and organic materials were extracted with methylene chloride, dried over magnesium sulfate and purified by column chromatography to afford the titled compound in a yield of 68.2%.

Example 67(d)

6-(β-Fucopyranosyl)-2-(sodium β-D-galactopyranosyl 3-sulfate)-1,3,5 trimethoxybenzene

To 2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)-6-(2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-1,3,5-trimethoxybenzene (prepared as described in Example 67(c) above) (1.12g, 1.10 mmol) in dimethylformamide (12ml) was added pyridinium sulfur trioxide (0.35g, 2.20mmol) at room temperature. After 1 hour, the mixture was evaporated under vacuum and the residue was dissolved in methanol and neutralized with 1N sodium hydroxide aqueous solution. Solvent was removed under vacuum and the

residue was through SEPHADEX® LH-20 (elution: water). Fractions containing pure material were evaporated and the residue was dissolved in 5% formic acid in methanol (50ml). To the solution was added palladium-black (0.63g) and the resultant solution was refluxed for 3 hours. The mixture was filtered through a celite pad and the filtrate was evaporated and subjected to lyophilization that afforded the freeze-dried product.

$[\alpha]_D$ = +5.8 (c=1.08, H_2O)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

6.60 (singlet, 1H),
4.85 - 4.72 (multiplet, 1H),
4.62 (doublet, J=9.4Hz, 1H),
4.54 (triplet, J=9.4Hz, 1H),
4.48 - 4.37 (multiplet, 1H),
3.92 (singlet, 3H),
3.91 (singlet, 3H),
3.79 (singlet, 3H),
3.71 (doublet of doublets, J=3.3, 9.4Hz, 1H),
4.00 - 3.66 (multiplet, 6H),
1.26 (doublet, J=6.5Hz, 3H).

Example 68

2-(β-L-Fucopyranosyl)-6-(sodium β-D-galactpyranosyl 2,-3,4,6-tetrasulfate)-1,3,5-trimethoxybenzene

To 6-(β-D-galactopyranosyl)-1,3,5-trimethoxy-2-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)benzene (prepared as described in Example 66(b) above) (187mg, 0.25mmol) in dimethylformamide (4ml) was added pyridinium sulfur trioxide (319mg, 2.00mmol). After stirring for 2 hours, ethyl acetate was added and the resultant white solid was decanted and dissolved in water and neutralized with 1N sodium hydroxide. The mixture was evaporated and the residue was through SEPHADEX® LH-20 (elution: water). Fractions containing pure materials were

evaporated and the residue was dissolved in 5% formic acid in methanol (50ml). To the solution was added palladium-black (0.63g) and the resultant solution was refluxed for 3 hours. The mixture was filtered through a celite pad and the filtrate was evaporated and subjected to lyophilization that afforded a freeze-dried product in a yield of 88.6%.

$[\alpha]_D$ + 3.6 (c=0.9, H_2O)

Nuclear Magnetic Resonance Spectrum 400MHz, D_2O)

6.54 (singlet, 1H),
5.56 (triplet, J=9.7Hz, 1H),
5.19 (doublet, J=2.7Hz, 1H),
4.88 (doublet, J=9.7Hz, 1H),
4.62 (doublet of doublets, J=2.7, 9.7Hz, 1H),
4.65 - 4.52 (multiplet, 2H),
4.32 (doublet of doublets, J=2.7, 10.5Hz, 1H),
4.28 (multiplet, 1H),
4.28 - 4.14 (multiplet, 2H),
3.94 (singlet, 3H),
3.91 (singlet, 3H),
3.81 (singlet, 3H),
4.01 - 3.66 (multiplet, 2H),
1.25 (doublet, J=6.4Hz, 3H).

Example 69

2-(β-D-Galactopyranosyl)-6-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)-1,3,5-trimethoxybenzene

A procedure similar to that described in Examples 66(b) and 68 above was followed, but using 2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-1,3,5-trimethoxybenzene (prepared as described in Example 60(a) above) and 2,3,4,6-tetra-O-benzyl-D-galactopyranosylfluoride to give the titled compound as a freeze-dried product in a yield of 53%.

$[\alpha]_D$ = +19.4 (c=0.7, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
6.54 (singlet, 1H,
5.19 (doublet, J=2.1Hz, 1H),
4.64 (doublet, J=9.4Hz, 1H),
4.59 (doublet of doublets, J=2.1, 8.5Hz, 1H),
4.33-4.18 (multiplet, 3H),
4.07 (doublet, J=3.3Hz, 1H),
3.94-3.71 (multiplet, 5H),
3.91, 3.83, 3.76 (3 x singlet, 9H).

Example 70
1-(β-L-Fucopyranosyl)-2,6-dimethoxy-5-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)naphthalene

A procedure similar to that described in Example 68 above was followed, but using 1-(β-D-galactopyranosyl)-2,6-dimethoxy-5-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl)naphthalene (prepared as described in Examples 66(a) and 66(b) above, but using β-D-galactose 1,2,3,4-pentaacetate, 2,6-dimethoxynaphthalene and 2,3,4-tri-O-benzyl-L-fucopyranosyl fluoride to give the titled compound as a freeze-dried in a yield of 35%.

$[\alpha]_D$ = +15 (c=0.26, water)

Nuclear Magnetic Resonance Spectrum (400MHz, WEFT, D_2O) δ ppm:
8.47 (doublet, J=10.3Hz, 1H),
8.43 (doublet, J=10.3Hz, 1H),
7.35 (doublet, J=9.5Hz, 1H),
7.21 (doublet, J=9.5Hz, 1H),
5.44 (doublet, J=9.9Hz, 1H),
5.12 (doublet, J=2.6Hz, 1H),
5.12 (doublet, J=9.2Hz, 1H),
5.01 (triplet, J=9.9Hz, 1H),
4.53 (doublet of doublets, J=2.6, 9.9Hz, 1H),
4.24-4.02 (multiplet, 3H),
4.12 (doublet, J=3.3Hz,1H),

3.86-3.70 (multiplet, 2H),
3.77, 3.75 (2 x singlet, 6H),
3.62 (doublet of doublets, J=3.3, 9.2Hz, 1H),
1.06 (doublet, J=6.6Hz, 3H).

Example 71
2,6-Dimethoxy-1-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)-5-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)naphthalene

A procedure similar to that described in Example 68 above was followed, but using 1-(tetra-O-acetyl-β-D-galactopyranosyl)-2,6-dimethoxy-5-(2,3,4-tri-O-benzyl-β-L-fucopyranosyl) naphthalene (prepared as described in Examples 66(a) and 66(b) above using 2,6-dimethoxynaphthalene instead of 1,3,5-trimethoxybenzene and the benzyl groups were removed by the method described in Example 68 above, before sulfation) to give the titled compound as a freeze-dried product in a yield of 99%.

$[\alpha]_D$ = +10.9 (c=0.47, water)

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
8.65 (doublet, J=9.6Hz, 1H),
8.64 (doublet, J=9.6Hz, 1H),
7.53 (doublet, J=9.6Hz, 1H),
7.52 (doublet, J=9.6Hz, 1H),
5.66 (doublet, J=10.0Hz, 1H),
5.60 (doublet, J=9.9Hz, 1H),
5.34 (doublet, J=2.5Hz, 1H),
5.27-5.19 (multiplet, 2H),
5.17 (doublet, J=2.6Hz, 1H),
4.76-4.68 (multiplet, 1H),
4.40 (doublet of doublets, J=3.6, 10.8Hz, 1H),
4.34 (doublet of doublets, J=3.6, 7.6Hz, 1H),
4.26 (doublet of doublets, J=7.6, 10.8Hz, 1H),

4.16 (quartet, J=6.4Hz, 1H),
3.99 (2 x singlet, 6H),
4.05-3.94 (multiplet, 1H),
1.37 (doublet, J=6.4Hz, 3H).

Example 72
Sodium cis 3-[4-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexyl sulfate

Example 72(a)
3-(4-Methoxyphenyl)-2-cyclohexen-1-one

Under an argon gas atmosphere, to a stirred hexane solution (20ml) of 2.5mM butyl lithium was slowly added a tetrahydrofuran solution (50ml) of 4-bromoanisole (9.35g, 50mmol) at -78°C. After being stirred for 30 minutes, a tetrahydrofuran solution (50ml) of 3-ethoxy-2-cyclohexen-1-one (7.0g, 50mmol) was added to the reaction solution and was stirred for additional 30 minutes. After being quenched by a 1N aqueous solution of hydrogen chloride, the reaction mixture was extracted with ethyl acetate and the extract was washed by a saturated aqueous solution of sodium bicarbonate and brine, then dried over sodium sulfate and evaporated. A purification by column chromatography with ethyl acetate / hexane (1 / 4) afforded 4.02g (40%) of the titled compound.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.52 (doublet, J=8.9Hz, 2H),
6.93 (doublet, J=8.9Hz, 2H),
6.40 (singlet, 1H),
3.85 (singlet, 3H),
2.76 (triplet, J=6.0Hz, 2H),
2.47 (triplet, J=7.1Hz, 2H),
2.14 (multiplet, 2H).

Example 72(b)
3-(4-Methoxyphenyl)cyclohexan-1-one

Under a hydrogen gas atmosphere, a reaction mixture of 3-(4-methoxyphenyl)-2-cyclohexen-1-one (prepared as described in Example 72(a) above) (4.04g, 20mmol), 10% palladium-carbon (400mg) and pyridine (3.16g, 20mmol) in ethyl acetate / ethanol (75ml / 5ml) was stirred for 16 hours at room temperature. After filtration of the catalyst through a celite pad, the filtrate was washed by a 1N aqueous solution of hydrogen chloride and brine, then dried over sodium sulfate and evaporated. A purification by column chromatography with ethyl acetate/hexane (1/4) afforded 3 compounds in a yield of 29.0%.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.13 (doublet, J=8.7Hz, 2H),
6.86 (doublet, J=8.7Hz, 2H),
3.79 (singlet, 3H),
2.96 (multiplet, 1H),
2.6-1.6 (multiplet, 8H).

In this reaction, the following Example 72(c) and Example 72(d) were also obtained as by-products.

Example 72(c)
Cis-3-(4-Methoxyphenyl)cyclohexan-1-ol
Contained as an oil in a yield of 47.5%.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.13 (doublet, J=8.6Hz, 2H),
6.85 (doublet, J=8.6Hz, 2H),
3.79 (singlet, 3H),
3.72 (multiplet,1H),
2.54 (multiplet, 1H),
2.2-1.2 (multiplet, 8H).

Example 72(d)

trans-3-(4-Methoxyphenyl)cyclohexan-1-ol

Obtained as an oil in a yield of 12.8%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.15 (doublet, J=8.7Hz, 2H),
6.85 (doublet, J=8.7Hz, 2H),
4.24 (multiplet, 1H),
3.80 (singlet, 3H),
2.96 (multiplet, 1H),
2.0-1.3 (multiplet, 8H).

Example 72(e)

3-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-one

A procedure similar to that described in Example 74(c) below was followed, but using 3-(4-methoxyphenyl)cyclohexan-1-one (prepared as described in Example 72(b) above) to give the titled compound as a foam in a yield of 59.2%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.30 (singlet, 1H),
7.11 (doublet, J=8.5Hz, 1H),
6.82 (doublet, J=8.5Hz, 1H),
5.49 (triplet, J=9.8Hz, 1H),
5.37 (doublet, J=3.3Hz, 1H),
5.21 (doublet of doublets, J=3.6, 10.1Hz,1H),
4.89 (doublet, J=9.9Hz, 1H),
3.96 (quartet, J=6.6Hz, 1H),
3.82 (singlet, 3H),
2.88 (multiplet, 1H),
2.6-1.7 (multiplet, 8H),
2.27, 1.99, 1.75 (3 x singlet, 9H),
1.22 (doublet, J=6.4Hz, 3H).

Example 72(f)

cis 3-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol

A procedure similar to that described in Example 74(d) below was followed, but using 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-one (prepared as described in Example 72(e) above) to give the titled compound as a foam in a yield of 59.2%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.27 (singlet, 1H),
7.11 (doublet, J=8.5Hz, 1H),
6.80 (doublet, J=8.5Hz, 1H),
5.51 (triplet, J=9.9Hz, 1H),
5.38 (doublet, J=3.4Hz, 1H),
5.21 (doublet of doublets, J=3.5, 10.0Hz, 1H),
4.89 (doublet, J=9.9Hz, 1H),
3.97 (quartet, J=6.4Hz, 1H),
3.82 (singlet, 3H),
3.73 (multiplet, 1H),
2.58 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
2.27, 1.99, 1.76 (3 x singlet, 9H),
1.23 (doublet, J=6.4Hz, 3H).

Example 72(g)

Sodium cis 3-[4-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexyl sulfate

A procedure similar to that described in Example 74(e) below was followed, but using cis 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described Example 72(f) above) to give the titled compound as a freeze-dried product in a yield of 93.8%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.45 (singlet, 1H),

7.30 (doublet, J=8.8Hz, 1H),
7.03 (doublet, J=8.8Hz, 1H),
4.70 (doublet, J=9.6Hz, 1H),
4.44 (multiplet, 1H),
4.0-3.8 (multiplet, 3H),
3.81 (singlet, 3H),
3.75 (doublet of doublets, J=3.3, 9.7Hz, 1H),
2.69 (multiplet, 1H),
2.3-1.3 (multiplet, 8H),
1.23 (doublet, J=6.6Hz, 3H).

Example 73
Sodium trans 3-[4-methoxy-3-(β-fucopyranosyl)phenyl]cyclohexyl sulfate

Example 73(a)
trans 1-Chloroacetoxy-3-(4-methoxyphenyl)cyclohexane

A procedure similar to that described in Example 79(b) below was followed, but using trans-3-(4-methoxyphenyl) cyclohexan-1-ol (prepared as described in Example 72(d) above) to give the titled compound as an oil in a yield of 85.8%.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.18 (doublet, J=8.7Hz, 1H),
6.86 (doublet, J 8.7Hz, 1H),
5.30 (multiplet, 1H),
4.11 (singlet, 2H),
3.76 (multiplet, 1H),
3.79 (singlet, 3H),
2.87 (multiplet, 1H),
2.1-1.4 (multiplet, 8H).

Example 73(b)
trans 1-Chloroacetoxy-3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexane

A procedure similar to that described in Example 79(d) below was followed, but using trans 1-chloroacetoxy-3-(4-methoxyphenyl)cyclohexane (prepared as described in Example 73(a) above) to give the titled compound as a foam in a yield of 70.2%.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.25 (singlet, 1H),
7.12 (doublet, J=8.5Hz, 1H),
6.82 (doublet, J=8.5Hz, 1H),
5.53 (multiplet, 1H),
5.3-5.2 (multiplet, 1H),
4.89 (multiplet, 1H),
4.15 (singlet, 2H),
3.98 (quartet, J=6.3Hz, 1H),
3.83 (singlet, 3H),
2.90 (multiplet, 1H),
2.3-1.2 (multiplet, 8H),
2.28, 2.01, 1.77 (3 x singlet, 9H),
1.24 (doublet, J=6.6Hz, 3H).

Example 73(c)
trans 3-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol

A procedure similar to that described in Example 79(f) below was followed, but using trans 1-chloroacetoxy-3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-fucopyranosyl)phenyl] cyclohexane (prepared as described in Example 73(b) above) to give the titled compound as a foam in a yield of 58.3%.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.29 (singlet, 1H),
7.11 (doublet, J=8.5Hz, 1H),

6.79 (doublet, J=8.5Hz, 1H),
5.51 (triplet, J=9.6Hz, 1H),
5.36 (doublet, J=3.2Hz, 1H),
5.22 (doublet of doublets, J=3.8, 9.6Hz, 1H),
4.89 (doublet, J=9.6Hz, 1H),
4.23 (multiplet, 1H),
3.96 (quartet, J=5.5Hz, 1H),
3.81 (singlet, 3H),
2.97 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
2.26, 1.99, 1.71 (3 x singlet, 9H),
1.22 (doublet, J=6.3Hz, 3H).

Example 73(d)

Sodium trans 3-[4-methoxy-3-(β-L-fucopyranosyl)phenyl] cyclohexyl sulfate

A procedure similar to that described in Example 79(g) below was followed, but using trans 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described in Example 73(c) above) to give the titled compound as a freeze-dried product in a yield of 58.2%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.46 (singlet, 1H),
7.30 (doublet, J=8.5Hz, 1H),
7.04 (doublet, J=8.5Hz, 1H),
4.70 (doublet, J=9.7Hz, 1H),
4.0-3.8 (multiplet, 3H),
3.82 (singlet, 3H),
3.76 (doublet of doublets, J=3.2, 9.7Hz, 1H),
2.92 (multiplet, 1H),
2.3-1.6 (multiplet, 8H),
1.24 (doublet, J=6.5Hz, 3H).

Example 74

Sodium cis 3-[3-methoxy-4-(β-L-fucopyranosyl)phenyl]cyclohexyl sulfate

Example 74(a)

3-(3-Methoxyphenyl)-2-cyclohexen-1-one

A procedure similar to that described in Example 72(a) above was followed, but using 3-bromoanisole to give the titled compound as an oil in a yield of 80.2%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.4-6.9 (multiplet, 4H),
6.41 (singlet, 1H),
3.84 (singlet, 3H),
2.76 (triplet, J=5.5Hz, 2H),
2.49 (triplet, J=7.1Hz, 2H),
2.17 (multiplet, 2H).

Example 74(b)

3-(3-Methoxyphenyl)cyclohexan-1-one

A procedure similar to that described in Example 72(b) above was followed, but using 3-(3-methoxyphenyl)-2-cyclohexen-1-one (prepared as described Example 74(a) above) to give the titled compound as an oil in a yield of 52.8%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.27 (multiplet, 1H),
6.80 (multiplet, 3H),
3.81 (singlet, 3H),
2.99 (multiplet, 1H),
2.7-1.7 (multiplet, 8H).

Example 74(c)
3-[3-Methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] cyclohexan-1-one

Under an argon gas atmosphere, a 1M methylene chloride solution (15ml, 15mmol) of tin(IV) chloride was added to a reaction mixture of 3-(3-methoxyphenyl)cyclohexan-1-one [prepared as described Example 74(b), above], (1.02g, 5mmol), L-fucose 1,2,3,4-tetraacetate (1.99g, 6mmol), and silver trifluoroacetate (1.65g, 7.5mmol) in methylene chloride (30ml) at 0°C. After being stirred for 8 hours at room temperature, the reaction was quenched by adding water. The insoluble material was filtered-off through a celite pad, and the filtrate was washed by a saturated aqueous solution of sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1 / 3) afforded 1.43g (60.0%) of the titled compound.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.42 (doublet, J=7.8Hz, 1H),
6.84 (doublet, J=7.8Hz, 1H),
6.68 (singlet, 1H),
5.49 (triplet, J=9.9Hz, 1H),
5.35 (doublet, J=3.3Hz, 1H),
5.20 (doublet of doublets, J=3.3, 9.9Hz, 1H),
4.89 (doublet, J=9.9Hz, 1H),
3.95 (quartet, J=6.6Hz, 1H),
3.83 (singlet, 3H),
2.99 (multiplet, 1H),
2.6-1.6 (multiplet, 8H),
2.23, 1.99, 1.77 (3 x singlet, 9H),
1.20 (doublet, J=6.2Hz, 3H).

Example 74(d)
cis 3-[3-Methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl]cyclohexan-1-ol

To an ethanol solution (15ml) of 3-[3-methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-one (prepared as described in Example 74(c) above) (1.40g, 2.9mmol) and p-toluenesulfonic acid-water (551mg, 2.9mmol), was added an ethanol solution (5ml) of sodium cyanoborohydride (182mg, 2.9mmol) at room temperature and was stirred for 15 minutes. After being quenched by water, the whole reaction mixture was extracted with ethyl acetate. The extract was washed by brine, dried over sodium sulfate, then concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate / hexane = 1 / 3 elution) which provided 680mg (48.5%) of the titled compound.
Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.38 (doublet, J=7.9Hz, 1H),
6.82 (doublet, J=7.9Hz, 1H),
6.69 (singlet, 1H),
5.50 (triplet, J=10.0Hz, 1H),
5.35 (doublet, J=2.7Hz, 1H),
5.20 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.88 (doublet, J=9.9Hz, 1H),
3.95 (quartet, J=5.1Hz, 1H),
3.82 (singlet, 3H),
3.76 (multiplet, 1H),
2.56 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
2.23, 1.99, 1.76 (3 x singlet, 9H),
1.20 (doublet, J=6.4Hz, 3H).

Example 74(e)

Sodium cis 3-[3-methoxy-4-(β-L-fucopyranosyl)phenyl]cyclohexylsulfate

To a pyridine solution (6ml) of cis 3-[3-methoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described in Example 74(d) above) (478mg, 1mmol), was added pyridinium sulfur trioxide (206mg, 1.3mmol) at room temperature and the mixture was stirred for 2 hours. After being quenched by adding methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (3-8% methanol-methylene chloride gradient solvent). The product was dissolved in methanol (5ml) and was hydrolyzed by adding a 1N sodium methoxide methanol solution (pH 9-10) at room temperature for 2 hours. After being concentrated under reduced pressure, the residue was again purified by using IATROBEADS™ column chromatography (10-20% methanol-methylene chloride gradient solvent) and was subjected to lyophilization which afforded 269mg of a freeze-dried product in a yield of 60.0%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.44 (doublet, J=8.2Hz, 1H),
7.02 (doublet, J=8.2Hz, 1H),
7.01 (singlet, 1H),
4.73 (doublet, J=9.8Hz, 1H),
4.47 (multiplet, 1H),
3.93 (triplet, J=9.8Hz, 1H),
3.86 (singlet, 3H),
3.76 (doublet of doublets, J=3.4, 9.7Hz, 1H),
2.75 (multiplet, 1H),
2.4-1.3 (multiplet, 8H),
1.24 (doublet, J=7.2Hz, 3H).

Example 75

Sodium cis 3-[2-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexyl sulfate

Example 75(a)

3-(2-Methoxyphenyl)-2-cyclohexen-1-one

A procedure similar to that described in Example 72(a) above was followed, but using 2-bromoanisole to give the titled compound as an oil in a yield of 78.7%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.4-6.9 (multiplet, 4H),
6.21 (singlet, 1H),
3.84 (singlet, 3H),
2.74 (triplet, J=5.7Hz, 2H),
2.49 (triplet, J=7.1Hz, 2H),
2.10 (multiplet, 2H).

Example 75(b)

3-(2-Methoxyphenyl)cyclohexan-1-one

A procedure similar to that described in Example 72(b) above was followed, but using 3-(2-methoxyphenyl)-2-cyclohexen-1-one (prepared as described in Example 75(a) above) to give the titled compound as an oil in a yield of 68.2%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:
7.26-6.84 (multiplet, 4H),
3.81 (singlet, 3H),
3.41 (multiplet, 1H),
2.6-1.7 (multiplet, 8H).

Example 75(c)

3-[2-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl] cyclohexan-1-one

A procedure similar to that described in Example 74(c) above was followed, but using 3-(2-methoxyphenyl) cyclohexane-1-one (prepared as described in Example 75(b) above) to give the titled compound as a foam in a yield of 52.5%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:

7.3-6.8 (multiplet, 3H),
5.4-5.3 (multiplet, 2H),
5.17 (doublet of doublets, J=3.2, 9.7Hz, 1H),
4.29 (doublet, J=9.7Hz, 1H),
3.95 (quartet, J=6.5Hz, 1H),
3.80 (singlet, 3H),
3.38 (multiplet, 1H),
2.6-1.7 (multiplet, 8H),
2.25, 1.99, 1.79 (3 x singlet, 9H),
1.23 (doublet, J=6.4Hz, 3H).

Example 75(d)

cis 3-[2-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) phenyl]cyclohexan-1-ol

A procedure similar to that described in Example 74(d) above was followed, but using 3-[2-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-one (prepared as described in Example 75(c) above) to give the titled compound as a foam in a yield of 74.7%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:

7.3-6.8 (multiplet, 3H),
5.4-5.1 (multiplet, 3H),
4.27 (doublet, J=9.7Hz, 1H),
3.94 (quartet, J=6.6Hz, 1H),
3.80 (singlet, 3H),

3.76 (multiplet, 1H),
3.00 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
2.25, 1.99, 1.79 (3 x singlet, 9H),
1.23 (doublet, J=6.4Hz, 3H).

Example 75(e)

Sodium cis 3-[2-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexyl sulfate

A procedure similar to that described in Example 74(e) above was followed, but using cis 3-(2-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described in Example 75(d) above) to give the titled compound as a freeze-dried product in a yield of 73.7%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.38 (multiplet, 1H),
7.27 (multiplet, 1H),
7.03 (doublet, J=8.7Hz, 1H),
4.45 (multiplet, 1H),
4.13 (doublet, J=9.0Hz, 1H),
3.9-3.7 (multiplet, 3H),
3.84 (singlet, 3H),
3.73 (doublet of doublets, J=3.2, 9.6Hz, 1H),
3.08 (multiplet, 1H),
2.3-1.3 (multiplet, 8H),
1.23 (doublet, J=6.4Hz, 3H).

Example 76

3-[4-Methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexan-1-acetic acid

Example 76(a)

Ethyl 3-(4-methoxphenyl)cyclohexan-1-acetate

Under an argon gas atmosphere, to a stirred tetrahydrofuran solution (2.2ml, 2.2mmol) containing 1M lithium bis(trimethylsilyl)amide was slowly added a tetrahydrofuran solution (5ml) of ethyl trimethylsilylacetate (350mg, 2.2mmol) at -78°C. After being stirred for 20 minutes, a tetrahydrofuran solution (5ml) of 3-(4-methoxyphenyl)-2-cyclohexen-1-one (prepared as described in Example 72(a) above) (404mg, 2mmol) was slowly added to the reaction solution and the resultant solution was stirred for additional 20 minutes. After being quenched by water, the reaction mixture was extracted with ethyl acetate and the extract was washed by a 1N aqueous solution of hydrogen chloride and brine, then dried over sodium sulfate and evaporated. A purification by column chromatography with ethyl acetate / hexane (1 / 10) afforded 427mg (yield: 78.5%) of the Peterson's products.

Under a hydrogen gas atmosphere, a reaction mixture of the Peterson's products (402mg, 1.48mmol) and 10% palladium-carbon (50mg) in ethanol (10ml) was stirred for 16 hours. After filtering-off the catalyst through a celite pad, the filtrate was concentrated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1 / 15) afforded 362mg (89.6%) of the titled compound.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$ δ ppm:

7.12 (doublet, J=8.7Hz, 1H),
6.83 (doublet, J=8.7Hz, 1H),
4.11 (quartet, J=7.1Hz, 2H),
3.78 (singlet, 3H),

2.53 (multiplet, 1H),
2.22 (doublet, J=7.0Hz, 2H),
2.0-1.0 (multiplet, 8H),
1.24 (triplet, J=7.1Hz, 3H).

Example 76(b)

Ethyl 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-acetate

Under an argon gas atmosphere, a 1M methylene chloride solution (12ml, 12mmol) of tin(IV) chloride was added to a reaction mixture of ethyl 3-(4-methoxyphenyl)-cyclohexan-1-acetate (prepared as described in Example 76(a) above) (1.0g, 3.62mmol), L-fucose 1,2,3,4-tetraacetate (1.32g, 4.0mmol), and silver trifluoroacetate (1.32g, 6.0mmol) in methylene chloride (30ml) at 0°C. After being stirred for 3 days at room temperature, the reaction was quenched by adding water. The insoluble material was filtered-off through a celite pad, and the filtrate was washed by a saturated aqueous solution of sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1 / 4) afforded 1.27g (64.0%) of the titled compound.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:

7.24 (singlet, 1H),
7.09 (doublet, J=8.5Hz, 1H),
6.78 (doublet, J=8.5Hz, 1H),
5.52 (triplet, J=10.0Hz, 1H),
5.36 (doublet, J=3.4Hz, 1H),
5.20 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.86 (doublet, J=9.9Hz, 1H),
4.13 (multiplet, 2H),
3.96 (quartet, J=6.6Hz, 1H),
3.81 (singlet, 3H),

2.6-1.0 (multiplet, 12H),
2.26, 1.99, 1.75 (3 x singlet, 9H),
1.25 (multiplet, 3H),
1.22 (doublet, J=6.6Hz, 3H).

Example 76(c)
3-[4-Methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexan-1-acetic acid

To a methanol solution (30ml) of ethyl 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-acetate (prepared as described in Example 76(b) above) (1.02g, 1.86mmol) was added a catalytic amount (0.1ml) of 28% sodium methoxide methanol solution. After being stirred for 2 hours, a 1N sodium hydroxide aqueous solution (5ml) was added to the reaction mixture and the resultant solution was stirred for 16 hours. The reaction mixture was acidified (pH 3) by adding a 1N aqueous solution of hydrogen chloride and the whole reaction mixture was concentrated under reduced pressure. A purification by column chromatography with 10% methanol-methylene chloride afforded 483mg (65.0%) of the titled compound.

Nuclear Magnetic Resonance Spectrum (400MHz, CD_3OD) δ ppm:
7.43 (singlet, 1H),
7.10 (doublet, J=8.8Hz, 1H),
6.87 (doublet, J=8.3Hz, 1H),
4.64 (doublet, J=9.6Hz, 1H),
3.9-3.7 (multiplet, 3H),
3.79 (singlet, 3H),
3.59 (doublet of doublets, J=2.9, 9.2Hz, 1H),
2.8-1.0 (multiplet, 12H),
1.26 (doublet, J=6.2Hz, 3H).

Example 77
cis 3-[4-Methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]cyclohexan-1-ol

Example 77(a)
3-[4-Methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexan-1-one

To a methanol solution (10ml) of 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-one (prepared as described in Example 72(e) above) (238mg, 0.5mmol) was added a catalytic amount (0.1ml) of 28% sodium methoxide methanol solution. After being stirred for 2 hours, AMBERLYST® 15 was added to the reaction mixture and neutralized it. After filtering-off the insoluble material, the whole reaction mixture was concentrated under reduced pressure. A purification by column chromatography with ethyl acetate afforded 162mg (92.5%) of the titled compound.

Nuclear Magnetic Resonance Spectrum (400MHz, CD_3OD) δ ppm:
7.43 (singlet, 1H),
7.11 (doublet, J=8.5Hz, 1H),
6.88 (doublet, J=8.5Hz, 1H),
4.65 (doublet, J=9.6Hz, 1H),
3.82 (triplet, J=9.6Hz, 1H),
3.80 (singlet, 3H),
3.73 (doublet, J=2.7Hz, 1H),
3.59 (doublet of doublets, J=3.4, 9.4Hz, 1H),
2.69 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
1.26 (doublet, J=6.4Hz, 3H).

Example 77(b)

3-[4-Methoxy-3-(sodium β-L-fucopyranosyl 2-3,4-trisulfate) phenyl]cyclohexan-1-one

To a pyridine solution (10ml) of 3-[4-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexan-1-one (prepared as described in Example 77(a) above) (385mg, 1.1mmol), was added pyridinium sulfur trioxide (636mg, 4mmol) at room temperature and the mixture was stirred for 16 hours. After being quenched by adding methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (methylene chloride / methanol / water = 70 / 25 3) and subjected to lyophilization that afforded 392mg (54.4%) of a freeze-dried product.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.26 (doublet, J=8.5Hz, 1H),
6.99 (doublet, J=8.5Hz, 1H),
5.04 (doublet, J=2.3Hz, 1H),
4.60 (doublet of doublets, J=2.1, 9.5Hz, 1H),
4.06 (quartet, J=6.5Hz, 1H),
3.84 (singlet, 3H),
3.04 (multiplet, 1H),
2.8-1.6 (multiplet, 8H),
1.30 (doublet, J=6.8Hz, 3H).

Example 77(c)

cis 3-[4-Methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]cyclohexan-1-ol

To a water solution (5ml) of 3-(4-methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]cyclohexan-1-one (prepared as described in Example 77(b) above) (345mg, 0.53mmol) was added a water solution (2ml) of sodium borohydride (20mg, 0.53mmol) at room temperature and the resultant solution was stirred for 30 minutes. After being

quenched by a 1N aqueous solution of hydrogen chloride, the reaction mixture was concentrated under reduced pressure. A purification by P-2 column chromatography using Bio-Gel P polyacrylamide gel with water elution afforded 189mg (54.7%) of the titled compound. Bio-Gel P gels are polyacrylamide beads for high resolution gel filtration. The gels are prepared by copolymerization of acrylamide and N,N'-methylene-bis-acrylamide. They provide efficient, gentle gel filtration of sensitive compounds. They are available from Bio-Rad Laboratories, Richmond, CA, USA.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.37 (multiplet, 1H),
7.24 (doublet, J=8.2Hz, 1H),
6.97 (doublet, J=8.4Hz, 1H),
5.03 (doublet, J=2.3Hz, 1H),
4.60 (doublet of doublets, J=1.4, 8.6Hz, 1H),
3.22 (multiplet, 1H),
4.04 (quartet, J=6.3Hz, 1H),
3.83 (singlet, 3H),
3.75 (multiplet, 1H),
2.60 (multiplet, 1H),
2.1-1.2 (multiplet, 8H),
1.30 (doublet, J=6.5Hz, 3H).

Example 78

Sodium cis 3-[4-methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]cyclohexylsulfate

Example 78(a)

Cis 3-[4-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexan-1-ol

To a methanol solution (5ml) of cis 3-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described in Example 72(f) above) (262mg, 0.55mmol) was

added a catalytic amount (0.1ml) of 28% sodium methoxide methanol solution. After being stirred for 2 hours, AMBERLYST® 15 was added to the reaction mixture and the reaction mixture was thus neutralized. After filtering-off the insoluble material, the whole reaction mixture was concentrated under reduced pressure. A purification by column chromatography with 10% methanol-methylene chloride afforded 168mg (87.0%) of the titled compound.

Nuclear Magnetic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

7.42 (singlet, 1H),
7.12 (doublet, J=8.8Hz, 1H),
6.88 (doublet, J=8.3Hz, 1H),
4.64 (doublet, J=9.6Hz, 1H),
3.9-3.5 (multiplet, 3H),
3.80 (singlet, 3H) ,
3.31 (multiplet, 1H),
2.55 (multiplet, 1H),
2.1-1.2 (multiplet, 8H),
1.26 (doublet, J=6.3Hz, 3H).

Example 78(b)

Sodium cis 3-[4-methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)phenyl]cyclohexylsulfate

To a pyridine solution (10ml) of cis 3-[4-methoxy-3-(β-L-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described in Example 78(a) above) (315mg, 0.89mmol), was added pyridinium sulfur trioxide (1.27g, 8mmol) at room temperature and the mixture was stirred for 16 hours. After being quenched by adding methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (methylene chloride / methanol / water pyridine = 70 / 25 / 3 / 0.5). Fractions containing pure compound were evaporated and dried under high vacuum. The product was

converted into a sodium salt by vigorous stirring with Dowex-50-X-8 (Na+) resin in methanol and subjected to lyophilization that afforded 291mg (37.9%) of a freeze-dried product.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.38 (multiplet, 1H),
7.26 (doublet, J=8.4Hz, 1H),
6.98 (doublet, J=8.8Hz, 1H),
5.04 (doublet, J=1.0Hz, 1H),
4.61 (doublet, J=7.8HZ, 1H),
4.45 (multiplet, 1H),
4.05 (quartet, J=6.3Hz, 1H),
3.84 (singlet, 3H),
2.63 (multiplet, 1H),
2.3-1.3 (multiplet, 8H),
1.31 (doublet, J=6.4Hz, 3H).

Example 79

Sodium trans 4-[4-methoxy-3-(β-L-fucopyranosyl)phenyl] cyclohexylsulfate

Example 79(a)

trans 4-(4-Methoxyphenyl)cyclohexan-1-ol and cis 4-(4-methoxyphenyl)cyclohexan-1-ol

To an ethanol solution (30ml) of 4-(4-methoxyphenyl)-cyclohexan-1-one (2.04g, 10mmol) was added sodium borohydride (380mg, 10mmol) at room temperature and the resultant solution was stirred for 30 minutes. The reaction mixture was extracted with ethyl acetate and the extract was washed with 1N aqueous solution of hydrogen chloride aqueous solution and brine. After being dried over sodium sulfate, the solvent was evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane / methylene chloride (1 / 3 / 1) afforded the following 2 compounds.

trans 4-(4-Methoxyphenyl)cyclohexan-1-ol

Yield : 74.5%

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:

7.12 (doublet, J=8.7Hz, 1H),
6.84 (doublet, J 8.7Hz, 1H),
3.79 (singlet, 3H),
3.68 (multiplet, 1H),
2.45 (multiplet, 1H),
2.1-1.3 (multiplet, 8H).

cis 4-(4-Methoxyphenyl)-cyclohexan-1-ol

Yield: 15.4%

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:

7.18 (doublet, J=8.6Hz, 1H),
6.85 (doublet, J 8.6Hz, 1H),
4.13 (multiplet, 1H),
3.80 (singlet, 3H),
2.50 (multiplet, 1H),
2.0-1.5 (multiplet, 8H).

Example 79(b)

trans 1-Chloroacetoxy-4-(4-methoxy-phenyl)cyclohexane

To a pyridine solution (10ml) of trans 4-(4-methoxyphenyl)cyclohexan-1-ol (prepared as described in Example 79(a) above) (1.50g, 7.3mmol) and chloroacetyl anhydride (1.71g, 10mmol) was added a catalytic amount of 4-dimethylaminopyridine and the whole reaction mixture was stirred for 5 hours at room temperature. The reaction mixture was extracted with ethyl acetate and the extract was washed with water, a 1N aqueous solution of hydrogen chloride, a saturated aqueous solution of sodium bicarbonate, and brine. After being dried over sodium sulfate, the solvent was

evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1 / 9) afforded 1.56g (80.7%) of the titled compound.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.12 (doublet, J=8.7Hz, 1H),
6.84 (doublet, J 8.7Hz, 1H),
4.87 (multiplet, 1H),
4.06 (singlet, 2H),
3.79 (singlet, 3H),
2.48 (multiplet, 1H),
2.2-1.4 (multiplet, 8H).

Example 79(c)

cis 1-Chloroacetoxy-4-(4-methoxyphenyl) cyclohexane

A procedure similar to that described in Example 79(b) above was followed, but using cis 4-(4-methoxyphenyl)cyclohexan-1-ol (prepared as described in Example 79(a) above) to give the titled compound as an oil in a yield of 92.5%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.12 (doublet, J=8.7Hz, 1H),
6.84 (doublet, J 8.7Hz, 1H),
4.93 (multiplet, 1H),
4.03 (singlet, 2H),
3.79 (singlet, 3H),
2.60 (multiplet, 1H),
2.2-1.2 (multiplet, 8H).

Example 79(d)

trans 1-Chloroacetoxy-4-[4-methoxy-3-(2,3,4-tri-O-acetyl-)β-L-fucopyranosyl)phenyl]cyclohexane

Under an argon gas atmosphere, a 1M methylene chloride solution (15ml, 15mmol) of tin(IV) chloride was added to a

reaction mixture of trans 1-chloroacetoxy-4-(4-methoxyphenyl)cyclohexane (prepared as described in Example 79(b) above) (1.25g, 4.4mmol), L-fucose 1,2,3,4-tetraacetate (1.66g, 5mmol) and silver trifluoroacetate (1.43g, 6.5mmol) in methylene chloride (40ml) at 0°C. After being stirred for 16 hours at room temperature, the reaction was quenched by adding water. The insoluble material was filtered-off through a celite pad, and the filtrate was washed by a saturated aqueous solution of sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1/4) afforded 1.60g of the titled compound in a yield of 65.5%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.26 (singlet, 1H),
7.09 (doublet, J=8.6Hz, 1H),
6.79 (doublet, J=8.6Hz, 1H),
5.49 (triplet, J=10.1Hz, 1H),
5.37 (doublet, J=3.4Hz, 1H),
5.20 (doublet of doublets, J=3.4, 10.1Hz, 1H),
4.89 (doublet, J=9.6Hz, 1H),
4.06 (singlet, 2H),
3.96 (quartet, J=6.5Hz, 1H),
3.81 (singlet, 3H),
2.53 (multiplet, 1H),
2.2-1.4 (multiplet, 8H),
2.26, 1.99, 1.75 (3 x singlet, 9H),
1.22 (doublet, J=6.4Hz, 3H).

Example 79(e)

cis 1-Chloroacetoxy-4-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexane

A procedure similar to that described in Example 79(d) above was followed, but using cis 1-chloroacetoxy-4-(4-methoxyphenyl)cyclohexane (prepared as described in Example 79(c) above) to give the titled compound as a foam in a yield of 71.6%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.27 (singlet, 1H),
7.09 (doublet, J=8.6Hz, 1H),
6.79 (doublet, J=8.6Hz, 1H),
5.49 (triplet, J=10.0Hz, 1H),
5.37 (doublet, J=3.5Hz, 1H),
5.22 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.93 (multiplet, 1H),
4.88 (doublet, J=10.0Hz, 1H),
4.04 (singlet, 2H),
3.96 (quartet, J=6.5Hz, 1H),
3.81 (singlet, 3H),
2.63 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
2.27, 1.99, 1.75 (3 x singlet, 9H),
1.23 (doublet, J=6.5Hz, 3H).

Example 79(f)

trans 4-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol

To an ethanol solution (20ml) of trans 1-chloroacetoxy-4-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexane (prepared as described in Example 79(d) above) (1.50g, 2.7mmol) and thiourea (610mg, 8mmol) was added collidine (360mg, 3mmol) and the resultant solution was stirred

for 16 hours at room temperature. The reaction mixture was extracted with ethyl acetate and the extract was washed with water, a 1N aqueous solution of hydrogen chloride and brine. After being dried over sodium sulfate, the solvent was evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1/3) afforded 620mg of the titled compound in a yield of 48.0%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.26 (singlet, 1H),
7.10 (doublet, J=8.4Hz, 1H),
6.78 (doublet, J=8.4Hz, 1H),
5.51 (triplet, J=10.2Hz, 1H),
5.36 (doublet, J=3.5Hz, 1H),
5.21 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.88 (doublet, J=10.0Hz, 1H),
3.96 (quartet, J=6.3Hz, 1H),
3.81 (singlet, 3H),
3.68 (multiplet, 1H),
2.47 (multiplet, 1H),
2.2-1.2 (multiplet, 8H),
2.26, 1.99, 1.75 (3 x singlet, 9H),
1.22 (doublet, J=6.6Hz, 3H).

Example 79(g)

Sodium trans 4-[4-methoxy-3-(β-L-fucopyranosyl)phenyl] cyclohexyl sulfate

To a pyridine solution (6ml) of trans 4-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)phenyl]cyclohexan-1-ol (prepared as described in Example 79(f) above) (600mg, 1.25mmol) was added pyridinium sulfur trioxide (230mg, 1.5mmol) at room temperature and the mixture was stirred for 2 hours. After being quenched by adding methanol, the solvent was concentrated under reduced pressure. The residue was purified

by using IATROBEADS™ column chromatography (3-8% methanol-methylene chloride gradient solvent). The product was dissolved in methanol (5ml) and was hydrolyzed by adding a IN sodium methoxide methanol solution (pH 9-10) at room temperature for 2 hours. After being concentrated under reduced pressure, the residue was again purified by using IATROBEADS™ column chromatography (10-20% methanol-methylene chloride gradient solvent) and was subjected to lyophilization that afforded 280mg of a freeze-dried product of the titled compound in a yield of 49.1%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.45 (singlet, 1H),
7.30 (doublet, J=8.5Hz, 1H),
7.03 (doublet, J=8.5Hz, 1H),
4.70 (doublet, J=9.7Hz, 1H),
4.41 (multiplet, 1H),
4.0-3.8 (multiplet, 3H),
3.82 (singlet, 3H),
3.76 (doublet of doublets, J=6.3, 9.6Hz, 1H),
2.57 (multiplet, 1H),
2.3-1.5 (multiplet, 8H),
1.24 (doublet, J=6.3Hz, 3H).

Example 80

Sodium cis 2-[4-methoxy-3-(β-L-fucopyranosyl)benzyl]cyclohexyl sulfate

Example 81

Sodium trans 2-[4-methoxy-3-(β-L-fucopyranosyl)benzyl] cyclohexyl sulfate

Example 80(a)

2-(4-Methoxybenzyl)cyclohexan-1-one

Under an argon gas atmosphere, to a 1M tetrahydrofuran solution (50ml, 50mmol) of lithium bis(trimethoxysilyl) amide was slowly added a tetrahydrofuran solution (75ml) of cyclohexanone (4.9g, 50mmol) at -78°C. After being stirred for 30 minutes, a tetrahydrofuran solution (75ml) of 4-methoxybenzylchloride (7.9g, 50mmol) was added to the reaction mixture and was stirred for 4 hours at -78°C. The reaction was quenched by adding water and was extracted with ethyl acetate. The extract was washed with a IN aqueous solution of hydrogen chloride and brine. After being dried over sodium sulfate, the solvent was evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1 / 9) afforded 4.95g of the titled compound in a yield of 45.4%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCL_3$) δ ppm:

7.08 (doublet, J=8.6Hz, 1H),
6.83 (doublet, J=8.6Hz, 1H),
3.79 (singlet, 3H),
3.17 (doublet of doublets, J=4.6, 13.8Hz, 1H),
2.6-1.2 (multiplet, 10H).

Example 80(b)

2-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) benzyl]cyclohexan-1-one

Under an argon gas atmosphere, a 1M methylene chloride solution (15ml, 15mmol) of tin(IV) chloride was added to a reaction mixture of 2-(4-methoxybenzyl)cyclohexan-1-one (prepared as described in Example 80(a) above) (1.09g, 5mmol), L-fucose 1,2,3,4-tetraacetate (1.99g, 6mmol), and silver trifluoroacetate (1.65g, 7.5mmol) in methylene chloride (30ml) at 0°C. After being stirred for 3 days at room temperature, the reaction was quenched by adding water. The insoluble material was filtered-off through a celite pad, and the filtrate was washed with a solution of sodium bicarbonate and brine, dried over sodium sulfate, then evaporated under reduced pressure. A purification by column chromatography with ethyl acetate/hexane (1/3) afforded 820mg of the titled compound in a yield of 33.5%.

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$,) δ ppm:

7.21 (singlet, 1H),
7.07 (multiplet, 1H),
6.78 (multiplet, 1H),
5.50 (triplet, J=10.1Hz, 1H),
5.37 (doublet, J=3.3Hz, 1H),
5.21 (doublet of doublets, J=3.3, 9.9Hz, 1H),
4.89 (doublet, J=10.2Hz, 1H),
3.97 (quartet, J=6.5Hz, 1H),
3.82 (singlet, 3H),
3.17 (multiplet, 1H),
2.6-1.2 (multiplet, 10H),
2.27, 2.00, 1.76 (3 x singlet, 9H),
1.22 (doublet, J=6.2Hz, 3H).

Example 80(c) and 81(a)

cis and trans 2-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-ol

To an ethanol solution (10ml) of 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-one (prepared as described in Example 80(b) above) (800mg, 1.6mmol) was added sodium borohydride (76mg, 2mmol) at room temperature and stirred for 30 minutes. The reaction mixture was quenched by a 1N aqueous solution of hydrogen chloride and was extracted with ethyl acetate. The extract was washed with a sodium bicarbonate aqueous solution and brine. After being dried over sodium sulfate, the solvent was evaporated under reduced pressure. A purification by column chromatography with ethyl acetate / hexane (1 / 3) afforded the following 2 compounds (Examples 80(c) and 81(a)).

Example 80(c)

cis 2-[4-Methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-ol

Yield : 40.0%

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.30 (singlet, 1H),
7.08 (doublet, J=8.4Hz, 1H),
6.79 (doublet, J=8.4Hz, 1H),
5.56 (triplet, J=10.1Hz, 1H),
5.36 (doublet, J=3.7Hz, 1H),
5.21 (doublet of doublets, J=3.8, 9.9Hz, 1H),
4.93 (doublet, J=9.9Hz, 1H),
3.97 (quartet, J=6.6Hz, 1H),
3.81 (singlet, 3H),
3.49 (multiplet, 1H),
2.66 (multiplet, 1H),
2.49 (multiplet, 1H),

1.8-1.2 (multiplet, 9H),
2.25, 1.99, 1.75 (3 x singlet, 9H),
1.21 (doublet, J=6.2Hz, 3H).

Example 81(a)

trans 2-[4-Methoxy-3-(2,3,4-tri-O-acetyl-3-β-fucopyranosyl)benzyl]cyclohexan-1-ol

Yield : 47.5%

Nuclear Magnetic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.26 (singlet, 1H),
7.08 (doublet, J=8.4Hz, 1H),
6.77 (doublet, J=8.4Hz, 1H),
5.53 (triplet, J=9.9Hz, 1H),
5.36 (doublet, J=2.9Hz, 1H),
5.20 (doublet of doublets, J=3.4, 10.1Hz, 1H),
4.87 (doublet, J=10.1Hz, 1H),
3.96 (quartet, J=6.4Hz, 1H),
3.81 (singlet, 3H),
3.28 (multiplet, 1H),
3.09 (multiplet, 1H),
2.31 (multiplet, 1H),
1.8-1.2 (multiplet, 9H),
2.26, 1.98, 1.74 (3 x singlet, 9H),
1.22 (doublet, J=6.4Hz, 3H).

Example 80(d)

Sodium cis 2-[4-methoxy-3-(β-L-fucopyranosyl)benzyl]cyclohexyl sulfate

To a pyridine solution (5ml) of cis 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-ol (prepared as described in Example 80(c) above) (246mg, 0.5mmol), was added pyridinium sulfur trioxide (95mg, 0.6mmol) at room temperature and the resultant mixture was stirred for 2 hours.

After being quenched by adding methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (3~8% methanol-methylene chloride gradient solvent). The product was dissolved in methanol (5ml) and was hydrolyzed by adding a IN sodium methoxide methanol solution (pH 9~10) at room temperature for 2 hours. After being concentrated under reduced pressure, the residue was again purified by using IATROBEADS™ column chromatography (10~20% methanol-methylene chloride gradient solvent) and subjected to lyophilization that afforded 125mg of a freeze-dried product of the titled compound in a yield of 53.4%.

Nuclear Magnetic Resonance Spectrum (400MHz, CD_3CD) δ ppm:

7.45 (singlet, 1H),
7.15 (doublet, J=8.4Hz, 1H),
6.87 (doublet, J=8.4Hz, 1H),
4.62 (doublet, J=9.7Hz, 1H),
4.44 (multiplet, 1H),
3.95 (triplet, J=9.6Hz, 1H),
3.79 (singlet, 3H),
3.75 (quartet, J=6.5Hz, 1H),
3.71 (doublet, J=3.6Hz, 1H),
3.58 (doublet of doublets, J=3.5, 9.5Hz, 1H),
2.79 (doublet of doublets, J=7.5, 13.6Hz, 1H),
2.28 (doublet of doublets, J=6.9, 13.6Hz, 1H),
2.31 (multiplet, 1H),
1.8-1.2 (multiplet, 8H),
1.25 (doublet, J=6.5Hz, 3H).

Example 81(b)

Sodium trans 2-[4-methoxy-3-(β-L-fucopyranosyl)benzyl] cyclohexyl sulfate

A procedure similar to that described in Example 80(d) above was followed, but using trans 2-(4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-ol (prepared as described in Example 81(a) above) to give the titled compound as a freeze-dried product in a yield of 59.0%.

Nuclear Magnetic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

7.38 (multiplet, 1H),
7.08 (multiplet, 1H),
6.86 (doublet, J=8.4Hz, 1H),
4.62 (doublet, J=9.6Hz, 1H),
4.07 (multiplet, 1H),
3.88 (triplet, J=9.6Hz, 1H),
3.80 (singlet, 3H),
3.75 (quartet, J=6.4Hz, 1H),
3.72 (doublet, J=3.0Hz, 1H),
3.59 (doublet of doublets, J=3.3, 9.3Hz, 1H),
3.22 (multiplet, 1H),
2.38 (multiplet, 1H),
2.25 (multiplet, 1H),
1.8-0.9 (multiplet, 8H),
1.27 (doublet, J=6.4Hz, 3H).

Example 82

Sodium trans 2-[4-methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)benzyl]cyclohexylsulfate

Example 82(a)

cis 2-[4-Methoxy-3-(β-L-fucopyranosyl)benzyl]cyclohexan-1-ol

To a methanol solution (3ml) of cis 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-ol (prepared

as described in Example 80(c) above) (72mg, 0.15mmol) was added a catalytic amount (0.1ml) of 28% sodium methoxide methanol solution. After being stirred for 2 hours, AMBERLYST® 15 was added to the reaction mixture and neutralized it. After filtering-off the insoluble material, the whole reaction mixture was concentrated under reduced pressure. A purification by column chromatography with 10% methanol-methylene chloride afforded 48mg of the titled compound in a yield of 90.5%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.39 (singlet, 1H),
7.09 (doublet, J=8.4Hz, 1H),
6.83 (doublet, J=8.4Hz, 1H),
4.65 (doublet, J=9.6Hz, 1H),
3.94 (triplet, J=9.4Hz, 1H),
3.85 (doublet, J=3.2Hz, 1H),
3.81 (singlet, 3H),
3.74 (doublet of doublets, J=3.2, 9.4Hz, 1H),
3.66 (multiplet, 1H),
2.60 (multiplet, 1H),
2.51 (multiplet, 1H),
1.8-1.2 (multiplet, 9H),
1.34 (doublet, J=6.5Hz, 3H).

Example 82(b)

trans 2-[4-Methoxy-3-(β-L-fucopyranosyl)benzyl]cyclohexan-1-ol

A procedure similar to that described in Example 82(a) above was followed, but using trans 2-[4-methoxy-3-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]cyclohexan-1-ol (prepared as described in Example 81(a) above) to give the titled compound as a foam in a yield of 87.8%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.34 (singlet, 1H),

7.08 (doublet, J=8.3Hz, 1H),
6.82 (doublet, J=8.3Hz, 1H),
4.63 (doublet, J=9.5Hz, 1H),
3.89 (triplet, J=9.3Hz, 1H),
3.82 (singlet, 3H),
3.72 (doublet of doublets, J=3.2, 9.2Hz, 1H),
3.26 (multiplet, 1H),
3.04 (multiplet, 1H),
2.0-1.0 (multiplet, 9H),
1.35 (doubletriplet, J=6.4Hz, 3H)

Example 82(c)

Sodium trans 2-[4-Methoxy-3-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)benzyl]cyclohexylsulfate

To a pyridine solution (10ml) of trans 2-[4-methoxy-3-(β-L-fucopyranosyl)benzyl]cyclohexan-1-ol [prepared as described in Example 83(b) above] (183mg, 0.5mmol), was added pyridinium sulfur trioxide (477mg, 3mmol) at room temperature and the mixture was stirred for 16 hours. After being quenched by adding methanol, the solvent was concentrated under reduced pressure. The residue was purified by using IATROBEADS™ column chromatography (methylene chloride / methanol / water / Pyridine = 70 / 25 / 3 / 0.5). Fractions containing pure compound were evaporated and dried under high vacuum. The product was converted into sodium salt by vigorous stirring with Dowex-50-X-8 (Na^+) resin in methanol and subjected to lyophilization that afforded 235mg of the freeze-dried product of the titled compound in a yield of 63.1%.

Nuclear Magnetic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.11 (doubletriplet, J=8.6Hz, 1H),
6.93 (doubletriplet, J=8.6Hz, 1H),
5.03 (doubletriplet, J=2.3Hz, 1H),
4.8-4.5 (multiplet, 3H),

4.03 (quartetriplet, J=6.3Hz, 1H),
3.83 (singlet, 3H),
2.9-1.0 (multiplet, 11H),
1.30 (doubletriplet, J=6.5Hz, 3H)

Example 83

1,4-Dimethoxy-2-(2,3,4-tri-o-acetyl-β-L-fucopyranosyl)-5-(tri-n-butylstannyl)benzene

Example 83(a)

5-Bromo-1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzene

To a solution of tetra-O-acetyl-L-fucose (9.96 mg, 30 mmol), silver trifluoroacetate (9.90 g, 45 mmol) and 1,4-dimethoxybenzene (6.21 mg, 45 mmol) in methylene chloride 100 ml was added a solution (1 M, 90 ml) of tin tetrachloride in methylene chloride, and the mixture was stirred at 0°C for one day. To the resulting solution was added a saturated aqueous sodium hydrogencarbonate solution to terminate the reaction. This mixture was passed through Celite and then extracted with methylene chloride, the organic layer was dried over anhydrous sodium sulfate, and the solvent was removed by evaporation under reduced pressure. The residue was purified by silica gel column chromatography to obtain 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzene (6.7 g, yield: 54.5 %).

In a methylene chloride solution (100 ml) was dissolved 4.1 g (10 mmol) of this compound. Bromine (0.62 ml, 12 mmol) was slowly added dropwise to this solution under ice cooling, and the mixture was stirred at 0°C for 2 hours. After completion of the reaction, water was added to the reaction mixture to terminate the reaction. The mixture was diluted with 100 ml of methylene chloride, and the diluted mixture was washed successively with a saturated aqueous sodium

hydrogencarbonate solution, an aqueous sodium thiosulfate solution and a saturated aqueous NaCl solution and then dried over magnesium sulfate. The solvent was removed by evaporation under reduced pressure.

The resulting oil was purified by silica gel column chromatography (ethyl acetate/hexane=1/4) to obtain 3.32 g (yield: 66 %) of the desired compound.

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.07 (1H, singlet),
7.03 (1H, singlet),
5.48 (1H, triplet, J=10.7 Hz),
5.37 (1H, doublet, J=2.9 Hz),
5.21 (1H, doublet of doublets, J=3.4, 10.1 Hz),
4.87 (1H, doublet, J=9.9 Hz),
3.97 (1H, quartet, J=6.6 Hz),
3.89 (3H, singlet),
3.80 (3H, singlet),
2.24, 1.99, 1.81 (9H, 3 x singlet),
1.22 (3H, doublet, J=6.6 Hz)

High resolution mass spectrum (FAB$^+$) $[M]^+$:
for $C_{20}H_{25}BrO_9$,
Calculated: 488.0682, Found: 488.0684

Optical rotation: $[\alpha]_D$=+16.4 (c=1.0, CH_2Cl_2)

Example 83(b)

1,4-Dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-5-(tri-n-butylstannyl)benzene

In 150 ml of toluene were suspended 5-bromo-1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzene (6.9 g, 14.1 mmol), tetrakistriphenylphosphinepalladium (810 mg, 0.7 mmol) and potassium carbonate (1.98 g, 15 mmol) under nitrogen gas stream. To the suspension was added bistributyltin (9.28 g, 16 mmol), and the mixture was refluxed under heating for 10 hours.

After completion of the reaction, the reaction mixture was diluted with 150 ml of ethyl acetate, and the diluted mixture was washed successively with water, an aqueous potassium fluoride solution, a saturated aqueous sodium hydrogencarbonate solution and a saturated aqueous NaCl solution and then dried over magnesium sulfate. The solvent was removed by evaporation under reduced pressure.

The resulting oil was purified by silica gel column chromatography (ethyl acetate/hexane=1/9) to obtain 7.60 g (yield: 77 %) of the desired compound.

Infrared absorption spectrum (liquid film method) cm^{-1}:

2956, 2928, 2872, 2852, 1752, 1483, 1464

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

6.88 (1H, singlet),
6.87 (1H, singlet),
5.56 (1H, triplet, J=9.9 Hz),
5.37 (1H, doublet, J=3.2 Hz),
5.21 (1H, doublet of doublets, J=3.3, 9.9 Hz),
4.90 (1H, doublet, J=10.0 Hz),
3.98 (1H, quartet, J=6.6 Hz),
3.81 (3H, singlet),
3.75 (3H, singlet),
2.24, 1.99, 1.78 (9H, 3 x singlet),
1.6-0.8 (27H, multiplet),
1.22 (3H, doublet, J=6.3 Hz)

High resolution mass spectrum (FAB$^+$) $[M+Na]^+$:

for $C_{32}H_{52}O_9NaSn^{116}$,

Calculated: 719.2526, Found: 719.2527

Optical rotation: $[\alpha]_D$=+15.3 (c=0.91, CH_2Cl_2)

Example 84

1,3-Dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-6-(tri-n-butylstannyl)benzene

Example 84(a)

6-Bromo-1,3-dimethoxy-4-(2,3,4-tri-o-acetyl-β-L-fucopyranosyl) benzene

The reaction of Example 83(a) was repeated analogously using L-fucose tetraacetate (16.6 g, 50 mmol) and 4-bromo-1,3-dimethoxybenzene (15.2 g, 70 mmol) to obtain 8.2 g (yield: 33.5 %) of the desired compound.

Melting point: 172 to 173°C

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

7.59 (1H, singlet),
6.41 (1H, singlet),
5.41 (1H, triplet, J=9.9 Hz),
5.34 (1H, doublet, J=4.3 Hz),
5.18 (1H, doublet of doublets, J=3.4, 10.0 Hz),
4.77 (1H, doublet, J=9.8 Hz),
3.92 (1H, quartet, J=6.6 Hz),
3.89 (3H, singlet),
3.85 (3H, singlet),
2.25, 1.99, 1.80 (9H, 3 x singlet),
1.21 (3H, doublet, J=6.6 Hz)

optical rotation: $[\alpha]_D$=+23.3 (c=0.56, CH_2Cl_2)

Example 84(b)

1,3-Dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-6-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using 6-bromo-1,3-dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) benzene (4.89 g, 10 mmol) to obtain 4.02 g (yield: 57.5 %) of the desired compound.

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.30 (1H, singlet),
6.35 (1H, singlet),
5.60 (1H, triplet, J=10.0 Hz),
5.34 (1H, doublet, J=2.3 Hz),
5.18 (1H, doublet of doublets, J=3.3, 10.0 Hz),
4.74 (1H, doublet, J=9.9 Hz),
3.93 (1H, quartet, J=6.6 Hz),
3.86 (3H, singlet),
3.75 (3H, singlet),
2.22, 1.99, 1.75 (9H, 3 x singlet),
1.7-0.8 (27H, multiplet),
1.20 (3H, doublet, J=6.3 Hz)
High resolution mass spectrum (FAB$^+$) $[M+Na]^+$:
for $C_{32}H_{52}O_9NaSn^{116}$,
Calculated: 719.2526, Found: 719.2534
Optical rotation: $[\alpha]_D$=+22.2 (c=0.8, CH_2Cl_2)

Example 85
1,4-Dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-(tri-n-butylstannyl)benzene

Example 85(a)
5-Bromo-1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzene

The reaction of the latter stage of Example 83(a) was repeated analogously using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzene (10.6 g, 22.7 mmol) to obtain 8.71 g (yield: 70.0 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
3479, 2964, 2943, 1751, 1495, 1370, 1219
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.08 (1H, singlet),

7.01 (1H, singlet),
5.52 (1H, doublet, J=3.4 Hz),
5.48 (1H, triplet, J=9.9 Hz),
5.21 (1H, doublet of doublets, J=3.4, 9.9 Hz),
4.89 (1H, doublet, J=9.9 Hz),
4.19-4.05 (3H, multiplet),
3.88 (3H, singlet),
3.80 (3H, singlet),
2.21, 2.04, 1.99, 1.81 (12H, 4 x singlet)
High resolution mass spectrum (FAB$^+$) $[M+H]^+$:
for $C_{22}H_{28}O_{11}Br^{79}$,
Calculated: 547.0815, Found: 547.0810
Optical rotation: $[\alpha]_D$=+22.2 (c=0.8, CH_2Cl_2)

Example 85(b)
1,4-Dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene

The reaction of Example 83(b) was repeated analogously using 5-bromo-1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzene (8.71 g, 15.9 mmol) to obtain 7.25 g (yield: 60.1 %) of the desired compound.
Infrared absorption spectrum (liquid film) cm^{-1}:
2956, 2928, 2872, 2851, 1754, 1483, 1464
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
6.88 (1H, singlet),
6.84 (1H, singlet),
5.55 (1H, triplet, J=10.0 Hz),
5.51 (1H, doublet, J=3.4 Hz),
5.20 (1H, doublet of doublets, J=3.4, 10.0 Hz),
4.91 (1H, doublet, J=10.0 Hz),
4.22-4.10 (3H, multiplet),
3.80 (3H, singlet),
3.73 (3H, singlet),

2.20, 2.02, 1.98, 1.76 (12H, 4 x singlet)
High resolution mass spectrum (FAB$^+$) [M+Na]$^+$:
for $C_{34}H_{54}O_{11}NaSn^{116}$,
Calculated: 777.2581, Found: 777.2585
Optical rotation: $[\alpha]_D$=-6.1 (c=1.0, CH_2Cl_2)

Example 86
1,3-Dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(tri-n-butylstannyl)benzene

Example 86(a)
6-Bromo-1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzene

The reaction of Example 83(a) was repeated analogously using D-galactose pentaacetate (10.9 g, 27.9 mmol) and 4-bromo-1,3-dimethoxybenzene (6.0 ml) to obtain the desired compound.

This compound was used for a next reaction without purification.

Example 86(b)
1,3-Dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using the above 6-bromo-1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzene to obtain 1.30 g (yield: 5.8 %) of the desired compound.
Infrared absorption spectrum (liquid film) cm^{-1}:
2956, 2929, 2872, 2852, 1754, 1593, 1579
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.31 (1H, singlet),
6.39 (1H, singlet),
5.13 (1H, triplet, J=9.9 Hz),
5.53 (1H, doublet, J=3.2 Hz),

5.20 (1H, doublet of doublets, J=3.2, 9.9 Hz),
4.79 (1H, doublet, J=9.9 Hz),
4.23-4.04 (3H, multiplet),
3.89 (3H, singlet),
3.79 (3H, singlet),
2.22, 2.05, 2.01, 1.79 (12H, 4 x singlet),
1.69-1.41 (6H, multiplet),
1.38-1.24 (6H, multiplet),
1.01 (6H, triplet, J=7.8 Hz),
0.91 (9H, triplet, J=7.2 Hz)
High resolution mass spectrum (FAB$^+$) [M+Na]$^+$:
for $C_{34}H_{54}O_{11}NaSn$,
Calculated: 781.2566, Found: 781.2559
optical rotation: $[\alpha]_D$=-12.0 (c=0.77, CH_2Cl_2)

Example 87
1,3-Dimethoxy-4-[methyl(5-acetamido-3,5-dideoxy-4,7,8,9-tetra-O-acetyl-α-D-glycero-D-galacto-2-nonulopyranosylonate]-6-(tri-n-butylstannyl)benzene

Example 87(a)
6-Bromo-1,3-dimethoxy-4-[methyl(5-acetamido-3,5-dideoxy-4,7,8,9-tetra-O-acetyl-α-D-glycero-D-galacto-2-nonulopyranosylate]benzene

The reaction of Example 83(a) was repeated analogously using 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-D-galacto-1-methyl-2-nonulosonate (21.32 g, 40 mmol) and 4-bromo-1,3-dimethoxybenzene (10.85 g, 50 mmol) to obtain 12.2 g (yield: 44.2 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
3377, 2956, 1746, 1372, 1232
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.73 (1H, singlet),

6.42 (1H, singlet),
5.52 (1H, doublet of doublets, J=5.2, 10.9 Hz),
5.47-5.41 (1H, multiplet),
5.35 (1H, doublet of doublets, J=2.0, 5.8 Hz),
5.28 (1H, doublet of triplets, J=3.0, 5.8 Hz),
4.41 (1H, doublet of doublets, J=3.0, 12.4 Hz),
4.23-4.10 (2H, multiplet),
3.93-3.80 (1H, multiplet),
3.90 (3H, singlet),
3.77 (3H, singlet),
3.71 (3H, singlet),
2.94 (1H, doublet of doublets, J=5.2, 13.3 Hz),
2.18, 2.10, 2.03, 2.01, 1.90 (15H, 5 x singlet),
1.85 (1H, triplet, J=13.3 Hz)
High resolution mass spectrum (FAB$^+$) $[M+H]^+$:
for $C_{28}H_{37}O_{14}NBr^{79}$,
Calculated: 690.1398, Found: 690.1382
Optical rotation: $[\alpha]_D$=-4.6 (c=0.72, CH_2Cl_2)

Example 87(b)
1,3-Dimethoxy-4-[methyl(5-acetamido-3,5-dideoxy-4,7,8,9-tetra-O-acetyl-α-D-glycero-D-galacto-2-nonulopyranosylate]-6-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using 6-bromo-1,3-dimethoxy-4-(5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-β-D-galacto-1-methyl-2-nonulosonate]benzene (173 mg, 0.251 mmol) to obtain 86.2 mg (yield: 38 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
3263, 3219, 3075, 3057, 3022, 3012, 2992, 2956, 2927, 1747
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.73 (1H, singlet),
6.33 (1H, singlet),

5.52 (1H, doublet of doublets, J=5.1, 10.6 Hz),
5.42-5.37 (2H, multiplet),
5.21 (1H, doublet of doublets, J=2.8, 6.4 Hz),
4.45 (1H, doublet of doublets, J=3.0, 12.4 Hz),
4.24-4.10 (2H, multiplet),
3.81-3.72 (1H, multiplet),
3.77 (3H, singlet),
3.75 (3H, singlet),
3.71 (3H, singlet),
2.89 (1H, doublet of doublets, J=5.1, 13.3 Hz),
2.17, 2.05, 1.99, 1.98, 1.90 (15H, 5 x singlet),
1.85 (1H, triplet, J=13.3 Hz),
1.73 (1H, doublet of doublets, J=11.3, 13.3 Hz),
1.60-1.48 (6H, multiplet),
1.40-1.23 (6H, multiplet),
1.07-1.01 (6H, multiplet),
0.90 (9H, triplet, J=7.2 Hz)
High resolution mass spectrum (FAB$^+$) $[M+Na]^+$:
for $C_{40}H_{63}O_{14}NaSn$,
calculated value: 920.3164, measured value: 920.3160
Angle of rotation: $[\alpha]_D$=-0.5 (c=0.82, CH_2Cl_2)

Example 88
1,4-Dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-5-(tri-n-butylstannyl)benzene

Example 88(a)
5-Bromo-1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)benzene

The reaction of the latter stage of Example 83(a) was repeated analogously using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)benzene (2.60 g, 5.22 mmol) to obtain 2.29 mg (yield: 80 %) of the desired compound.

Infrared absorption spectrum (KBr) cm^{-1}:
2947, 1754
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.07 (1H, singlet),
6.95 (1H, singlet),
5.36 (1H, triplet, J=9.2 Hz),
5.30 (1H, triplet, J=9.2 Hz),
5.23 (1H, triplet, J=9.2 Hz),
4.92 (1H, doublet, J=9.2 Hz),
4.27 (1H, doublet of doublets, J=4.9, 12.4 Hz),
4.14 (1H, doublet of doublets, J=2.1, 12.4 Hz),
3.87 (3H, singlet),
3.87-3.77 (1H, multiplet),
3.80 (3H, singlet),
2.07, 2.06, 2.01, 1.80 (12H, 4 x singlet)
High resolution mass spectrum (FAB$^+$) $[M]^+$:
for $C_{22}H_{27}BrO_{11}$,
Calculated: 546.0737, Found: 546.0739
Optical rotation: $[\alpha]_D$=-18.7 (c=1.0, $CHCl_3$)

Example 88(b)
1,4-Dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-5-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using 5-bromo-1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)benzene (272 mg, 0.50 mmol) to obtain 251 mg (yield: 67 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
2956, 2927, 2872, 2851, 1755
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
6.88 (1H, singlet),
6.79 (1H, singlet),
5.44-5.19 (3H, multiplet),

4.95 (1H, doublet, J=9.7 Hz),
4.27 (1H, doublet of doublets, J=4.7, 12.3 Hz),
4.14 (1H, doublet of doublets, J=2.2, 12.3 Hz),
3.90-3.80 (1H, multiplet),
3.81 (3H, singlet),
3.73 (3H, singlet),
2.07, 2.06, 2.01, 1.78 (12H, 4 x singlet),
1.59-1.42 (6H, multiplet),
1.31 (6H, multiplet),
1.02 (6H, triplet, J=7.4 Hz),
0.87 (9H, triplet, J=7.4 Hz)
High resolution mass spectrum (FAB$^+$) $[M+Na]^+$:
for $C_{34}H_{54}O_{11}NaSn$,
Calculated: 781.2566, Found: 781.2559
Optical rotation: $[\alpha]_D$=-53.1 (c=0.85, $CHCl_3$)

Example 89
1,4-Dimethoxy-2-(3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-5-(tri-n-butylstannyl)benzene

Example 89(a)
5-Bromo-1,4-dimethoxy-2-(3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)benzene

The reaction of the latter stage of Example 83(a) was repeated analogously using 1,4-dimethoxy-2-(3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)benzene (1.11 g, 2.0 mmol) to obtain 1.28 mg (yield: 89 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
2936, 1751, 1721
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.88-7.65 (4H, multiplet),
7.04 (1H, singlet),
6.82 (1H, singlet),

6.13 (1H, triplet, J=10.0 Hz),
5.64 (1H, doublet, J=10.0 Hz),
5.29 (1H, triplet, J=10.0 Hz),
4.59 (1H, triplet, J=10.0 Hz),
4.35 (1H, doublet of doublets, J=4.9, 12.3 Hz),
4.20 (1H, doublet of doublets, J=2.2, 12.3 HZ),
4.10-4.00 (1H, multiplet),
3.88 (3H, singlet),
3.41 (3H, singlet),]
2.10, 2.08, 1.87 (9H, 3 x singlet)
High resolution mass spectrum (FAB$^+$)[M]$^+$:
for $C_{28}H_{28}BrNO_{11}$,
Calculated: 633.0846, Found: 633.0845
Optical rotation: $[\alpha]_D$=-75.1 (c=0.23, $CHCl_3$)

Example 89(b)
1,4-Dimethoxy-2-(3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-5-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using 5-bromo-1,4-dimethoxy-2-(3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)benzene (319 mg, 0.50 mmol) to obtain 195 mg (yield: 46 %) of the desired compound.
Infrared absorption spectrum (liquid film) cm^{-1}:
2956, 2928, 2871, 2852, 1752, 1722
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.87-7.56 (4H, multiplet),
6.89 (1H, singlet),
6.62 (1H, singlet),
6.13 (1H, triplet, J=10.0 Hz),
5.68 (1H, doublet, J=10.0 Hz),
5.30 (1H, triplet, J=10.0 Hz),
4.65 (1H, triplet, J=10.0 Hz),
4.34 (1H, doublet of doublets, J=4.7, 12.2 Hz),

4.21 (1H, doublet of doublets, J=2.1, 12.2 Hz),
4.10-3.98 (1H, multiplet),
3.74 (3H, singlet),
3.45 (3H, singlet),
2.10, 2.07, 1.87 (9H, 3 x singlet),
1.50-1.35 (6H, multiplet),
1.35-1.18 (6H, multiplet),
0.95 (6H, triplet, J=7.1 Hz),
0.83 (9H, triplet, J=7.2 Hz)
High resolution mass spectrum (FAB$^+$)[M+K]$^+$:
for $C_{40}H_{55}O_{11}NKSn$,
Calculated: 880.2453, Found: 880.2441
Optical rotation: $[\alpha]_D$=-58.4 (c=0.55, $CHCl_3$)

Example 90
1,4-Dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)-5-(tri-n-butylstannyl)benzene

Example 90(a)
5-Bromo-1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)benzene

The reaction of the latter stage of Example 83(a) was repeated analogously using 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)benzene (960 mg, 2.34 mmol) to obtain 1.10 g (yield: 96 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
2983, 2940, 2851, 1750
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.07 (1H, singlet),
7.00 (1H, singlet),
5.57 (1H, doublet of doublets, J=1.1, 3.3 Hz),
5.25 (1H, doublet of doublets, J=3.3, 9.9 Hz),
5.14 (1H, triplet, J=9.9 Hz),

4.97 (1H, singlet),
3.87 (3H, singlet),
3.79 (3H, singlet),
3.75-3.62 (1H, multiplet),
2.08, 1.99, 1.91 (9H, 3 x singlet),
1.34 (3H, doublet, J=6.1 Hz)
High resolution mass spectrum (FAB$^+$)[M]$^+$:
for $C_{20}H_{25}BrO_9$,
Calculated: 488.0682, Found: 488.0680
Optical rotation: $[\alpha]_D$=+33.9 (c=1.0, $CHCl_3$)

Example 90(b)
1,4-Dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)-5-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using 5-bromo-1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-rhamnopyranosyl)benzene (485 mg, 0.991 mmol) to obtain 385 mg (yield: 56 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
2953, 2928, 2869, 2854, 1750
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
6.94 (1H, singlet),
6.79 (1H, singlet),
5.56 (1H, doublet, J=3.3 Hz),
5.27 (1H, doublet of doublets, J=3.3, 9.9 Hz),
5.15 (1H, triplet, J=9.9 Hz),
5.03 (1H, singlet),
3.79 (3H, singlet),
3.74 (3H, singlet),
3.75-3.62 (1H, multiplet),
2.08, 1.98, 1.89 (9H, 3 x singlet),
1.58-1.40 (6H, multiplet),
1.40-1.20 (9H, multiplet),

1.00 (6H, triplet, J=8.1 Hz),
0.87 (9H, triplet, J=7.2 Hz)
High resolution mass spectrum (FAB$^+$)[M+K]$^+$:
for $C_{32}H_{52}O_9KSn$,
Calculated: 735.2266, Found: 735.2246
Optical rotation: $[\alpha]_D$=+32.6 (c=0.99, $CHCl_3$)

Example 91
1,4-Dimethoxy-2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-5-(tri-n-butylstannyl)benzene

Example 91(a)
5-Bromo-1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)benzene

The reaction of the latter stage of Example 83(a) was repeated analogously using 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)benzene (200 mg, 0.50 mmol) to obtain 232 mg (yield: 91.3 %) of the desired compound.
Infrared absorption spectrum (thin film) cm^{-1}:
3014, 2947, 2852, 1755
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.27 (1H, singlet),
7.06 (1H, singlet),
5.35 (1H, triplet, J=9.4 Hz),
5.27 (1H, triplet, J=9.4 Hz),
5.22-4.97 (1H, multiplet),
4.81 (1H, doublet, J=9.4 Hz),
4.21 (1H, doublet of doublets, J=5.5, 11.0 Hz),
3.86 (3H, singlet),
3.79 (3H, singlet),
3.46 (1H, triplet, J=11.0 Hz),
2.06, 2.03, 1.80 (9H, 3 x singlet)
High resolution mass spectrum (FAB$^+$)[M]$^+$:

for $C_{19}H_{23}BrO_9$,
Calculated: 474.0526, Found: 474.0523
Optical rotation: $[\alpha]_D$=-28.6 (c=0.86, $CHCl_3$)

Example 91(b)
1,4-Dimethoxy-2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-5-(tri-n-butylstannyl)benzene

The reaction of Example 83(b) was repeated analogously using 5-bromo-1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)benzene (232 mg, 0.49 mmol) to obtain 100 mg (yield: 29.8 %) of the desired compound.
Infrared absorption spectrum (liquid film) cm^{-1}:
2956, 2927, 2871, 2853, 1758
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
6.87 (1H, singlet),
6.78 (1H, singlet),
5.36 (1H, triplet, J=9.3 Hz),
5.31 (1H, triplet, J=9.3 Hz),
5.23-5.09 (1H, multiplet),
4.84 (1H, doublet, J=9.3 Hz),
4.21 (1H, doublet of doublets, J=5.8, 11.0 Hz),
3.81 (3H, singlet),
3.72 (3H, singlet),
3.48 (1H, triplet, J=11.0 Hz),
2.06, 2.03, 1.78 (9H, 3 x singlet),
1.57-1.42 (6H, multiplet),
1.42-1.23 (6H, multiplet),
1.02 (6H, triplet, J=8.0 Hz),
0.87 (9H, triplet, J=7.3 Hz)
High resolution mass spectrum (FAB$^+$)$[M+K]^+$:
for $C_{31}H_{50}O_9KSn$,
Calculated: 721.2109, Found: 721.2078
Optical rotation: $[\alpha]_D$=-30.3 (c=0.73, $CHCl_3$)

Example 92
4-Methyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(tri-n-butylstannyl)anisole

Example 92(a)
6-Bromo-4-methyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)anisole

The reaction of the latter stage of Example 83(a) was repeated analogously using 4-methyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)anisole (1.10 g, 2.43 mmol) to obtain 602 mg (yield: 46.6 %) of the desired compound.
Infrared absorption spectrum (KBr) cm^{-1}:
2938, 1753
Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:
7.36 (1H, doublet, J=1.9 Hz),
7.21 (1H, doublet, J=1.9 Hz),
5.55 (1H, triplet, J=10.0 Hz),
5.53 (1H, doublet, J=3.3 Hz),
5.20 (1H, doublet of doublets, J=3.3, 10.0 Hz),
4.79 (1H, doublet, J=10.0 Hz),
4.23-4.05 (3H, multiplet),
3.86 (3H, singlet),
2.31 (3H, singlet),
2.23, 2.02, 2.00, 1.81 (12H, 4 x singlet)
High resolution mass spectrum (FAB$^+$)$[M+H]^+$:
for $C_{22}H_{28}BrO_{10}$,
Calculated: 531.0866, Found: 531.0867
Optical rotation: $[\alpha]_D$=-11.5 (c=0.13, $CHCl_3$)

Example 92(b)

4-Methyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(tri-n-butylstannyl)anisole

The reaction of Example 83(b) was repeated analogously using 6-bromo-4-methyl-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl) anisole (602 mg, 1.13 mmol) to obtain 34 mg (yield: 4.1 %) of the desired compound.

Infrared absorption spectrum (liquid film) cm^{-1}:

2957, 2925, 2872, 2855, 1754

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

7.24 (1H, doublet, J=1.9 Hz),
7.13 (1H, doublet, J=1.9 Hz),
5.58 (1H, triplet, J=10.1 Hz),
5.53 (1H, doublet, J=3.5 Hz),
5.20 (1H, doublet of doublets, J=3.5, 10.1 Hz),
4.80 (1H, doublet, J=10.1 Hz),
4.22-4.05 (3H, multiplet),
3.71 (3H, singlet),
2.32, 2.24, 2.01, 1.99, 1.75 (15H, 5 x singlet),
1.57-1.43 (6H, multiplet),
1.43-1.24 (6H, multiplet),
1.07 (6H, triplet, J=8.2 Hz),
0.88 (9H, triplet, J=7.3 Hz)

High resolution mass spectrum (FAB^+) $[M+K]^+$:

for $C_{34}H_{54}O_{10}KSn$,

Calculated: 777.2372, Found: 777.2357

Optical rotation: $[\alpha]_D$=+6.9 (c=0.26, $CHCl_3$)

Example 93

2,6-Dimethoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-(tri-n-butylstannyl)naphthalene

Example 93(a)

5-Bromo-2,6-dimethoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)naphthalene

The reaction of the latter stage of Example 83(a) was repeated analogously using 5-bromo-2,6-dimethoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)naphthalene (1.13 g, 2.18 mmol) to obtain 889 mg (yield: 68.3 %) of the desired compound.

Infrared absorption spectrum (KBr) cm^{-1}:

2942, 2844, 1753

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

8.66 (1H, doublet, J=9.5 Hz),
8.28 (1H, doublet, J=9.5 Hz),
7.29 (1H, doublet, J=9.5 Hz),
7.27 (1H, doublet, J=9.5 Hz),
5.91 (1H, triplet, J=9.7 Hz),
5.63 (1H, doublet, J=3.2 Hz),
5.59 (1H, doublet, J=9.7 Hz),
5.29 (1H, doublet of doublets, J=3.2, 9.7 Hz),
4.33-4.10 (3H, multiplet),
4.02 (3H, singlet),
3.95 (3H, singlet),
2.34, 2.04, 1.99, 1.68 (12H, 4 x singlet)

High resolution mass spectrum (FAB^+) $[M]^+$:

for $C_{26}H_{29}BrO_{11}$,

Calculated: 596.0873, Found: 596.0869

Optical rotation: $[\alpha]_D$=-44.7 (c=0.73, $CHCl_3$)

Example 93(b)

2,6-Dimethoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-(tri-n-butylstannyl)naphthalene

The reaction of Example 83(b) was repeated analogously using 5-bromo-2,6-dimethoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)naphthalene (565 mg, 0.95 mmol) to obtain 148 mg (yield: 19.3 %) of the desired compound.

Infrared absorption spectrum (liquid film) cm^{-1}:

2956, 2928, 2871, 2853, 1754

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

8.64 (1H, doublet, J=9.3 Hz),
7.76 (1H, doublet, J=9.3 Hz),
7.19 (1H, doublet, J=9.3 Hz),
7.16 (1H, doublet, J=9.3 Hz),
5.95 (1H, triplet, J=10.1 Hz),
5.62 (1H, doublet, J=3.2 Hz),
5.59 (1H, doublet, J=10.1 Hz),
5.28 (1H, doublet of doublets, J=3.2, 10.1 Hz),
4.32-4.20 (1H, multiplet),
4.20-4.08 (2H, multiplet),
3.92 (3H, singlet),
3.87 (3H, singlet),
2.34, 2.04, 1.99, 1.68 (12H, 4 x singlet),
1.57-1.43 (6H, multiplet),
1.43-1.23 (6H, multiplet),
1.15 (6H, triplet, J=8.2 Hz),
0.87 (9H, triplet, J=7.2 Hz)

High resolution mass spectrum (FAB$^+$) $[M+K]^+$:

for $C_{30}H_{56}O_{11}KSn$,

Calculated: 843.2477, Found: 843.2469

Optical rotation: $[\alpha]_D$=-35.2 (c=0.81, $CHCl_3$)

Example 94

2-Methoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(tri-n-butylstannyl)naphthalene

Example 94(a)

6-Bromo-2-methoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)naphthalene

The reaction of Example 83(a) was repeated analogously using β-D-galactose pentaacetate (2.0 g, 5.12 mmol) and 2-bromo-6-methoxynaphthalene (2.42 g, 10.2 mmol) to obtain 888 mg (yield: 30.6 %) of the desired compound.

Infrared absorption spectrum (KBr) cm^{-1}:

2942, 1753, 1591

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

8.55 (1H, doublet, J=9.3 Hz),
7.91 (1H, doublet, J=2.0 Hz),
7.72 (1H, doublet, J=9.1 Hz),
7.54 (1H, doublet of doublets, J=2.0, 9.3 Hz),
7.22 (1H, doublet, J=9.1 Hz),
5.88 (1H, triplet, J=9.8 Hz),
5.62 (1H, doublet, J=3.2 Hz),
5.57 (1H, doublet, J=9.8 Hz),
5.28 (1H, doublet of doublets, J=3.2, 9.8 Hz),
4.31-4.19 (1H, multiplet),
4.19-4.07 (2H, multiplet),
3.95 (3H, singlet),
2.33, 2.05, 1.99, 1.68 (12H, 4 x singlet)

High resolution mass spectrum (FAB$^+$) $[M]^+$:

for $C_{25}H_{27}BrO_{10}$,

Calculated: 566.0788, Found: 566.0796

Optical rotation: $[\alpha]_D$=-13.7 (c=0.41, $CHCl_3$)

Example 94(b)

2-Methoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-(tri-n-butylstannyl)naphthalene

The reaction of Example 83(b) was repeated analogously using 6-bromo-2-methoxy-1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)naphthalene (830 mg, 1.46 mmol) to obtain 315 mg (yield: 27.7 %) of the desired compound.

Infrared absorption spectrum (thin film) cm^{-1}:

2957, 2926, 2872, 2853, 1754

Nuclear magnetic resonance spectrum (270 MHz, $CDCl_3$): δ ppm:

8.56 (1H, doublet, J=8.5 Hz),
7.83 (1H, singlet),
7.77 (1H, doublet, J=9.1 Hz),
7.52 (1H, doublet, J=8.5 Hz),
7.19 (1H, doublet, J=9.1 Hz),
5.96 (1H, triplet, J=9.9 Hz),
5.62 (1H, doublet, J=3.2 Hz),
5.59 (1H, doublet, J=9.9 Hz),
5.30 (1H, doublet of doublets, J=3.2, 9.9 Hz),
4.35-4.23 (1H, multiplet),
4.20-4.07 (2H, multiplet),
3.94 (3H, singlet),
2.36, 2.05, 1.99, 1.69 (12H, 4 x singlet),
1.66-1.50 (6H, multiplet),
1.47-1.23 (6H, multiplet),
1.10 (6H, triplet, J=8.1 Hz),
0.91 (9H, triplet, J=7.2 Hz)

High resolution mass spectrum (FAB^+) $[M+H]^+$:

for $C_{37}H_{55}O_{10}Sn$,

Calculated: 775.2813, Found: 775.2804

Optical rotation: $[\alpha]_D$=-39.4 (c=1.03, $CHCl_3$)

Example 95

4-[2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-benzoic acid Methyl ester

A solution of 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene (200.5mg, 0.265mmol), methyl 4-(bromomethyl)-benzoate (219.5mg, 0.958mmol), [1,2-bis(diphenylphosphino)ethane] dichloropalladium (14.9mg, 0.0259mmol) and sodium carbonate (57.6mg, 0.543mmol) in toluene was refluxed for 8 hours under a nitrogen atmosphere.

The resulting mixture was diluted with ethyl acetate and washed with a saturated aqueous solution of potassium fluoride, sodium bicarbonate and brine, dried over magnesium sulfate, then evaporated under reduced pressure.

A purification of the resulting residue by column chromatography with ethyl acetae / hexane (1 / 3) afforded 127.8mg of the titled compound in a yield of 78.1%.

$[\alpha]_D^{23}$ = -4.2 (C=0.83, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.93 (doublet, J=8.2Hz, 2H),
7.23 (doublet, J=8.2Hz, 2H),
6.95 (singlet, 1H),
6.60 (singlet, 1H),
5.53 (triplet, J=10.0Hz, 2H),
5.21 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.91 (doublet, J=10.0Hz, 1H),
4.22-3.92 (multiplet, 5H),
3.90 (singlet, 3H),
3.79 (singlet, 3H),
3.72 (singlet, 3H),
2.21 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),

1.79 (singlet, 3H)

Example 96

4-[2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)-benzyl]-benzoic acid

To a methanol solution (3ml) of 4-[2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-benzoic acid methyl ester (127.8mg, 0.207mmol) was added a few drops of 28% sodium methoxide methanol solution. After being stirred for 8 hours, the whole reaction mixture was neutralized by adding a small amount of Amberlyst 15 (acidic ion-exchange resin). An insoluble material was filtered off through celite pad and the filtrate was concentrated under reduced pressure.

A purification of the resulting residue by PLC plate (silicagel 60) with ethyl acetae / methanol / water (15 / 3 / 0.5) afforded the deacetylated compound.

To the above product was added 3ml of 1N sodium hydroxide solution and stirred for 6 hours at room temperature. After being acidified by adding 1N solution of hydrochrolic acid, the whole reaction mixture was concentrated under reduced pressure.

A purification of the resulting residue by PLC plate (silicagel 60) with ethyl acetae / methanol / water (15 / 3 / 1) and lyophilization afforded 63.3mg of the titled compound in a yield of 70.5%.

$[\alpha]_D^{23}$ = +12 (C=0.29, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.79 (doublet, J=8.1Hz, 2H),
7.33 (doublet, J=8.1Hz, 2H),
7.23 (singlet, 1H),
7.03 (singlet, 1H),
4.72 (doublet, J=9.7Hz, 1H),
4.08-4.05 (multiplet, 3H),
3.92 (triplet, J=9.7Hz, 1H),

3.83-3.75 (multiplet, 4H),
3.80 (singlet, 6H)

Example 97

3-[2',5'-Dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and methyl 3-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 40.1%.

$[\alpha]_D^{23}$ = -5.6 (C=0.64, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.89-7.85 (multiplet, 3H),
7.35-7.32 (multiplet, 2H),
6.95 (singlet, 1H),
6.61 (singlet, 1H),
5.53 (triplet, J=10.0Hz, 1H),
5.52 (doublet; J=3.3Hz, 1H),
5.21 (doublet of doublets, J=3.3, 10.0Hz, 1H),
4.91 (doublet, J=10.0Hz, 1H),
4.18-3.94 (multiplet, 5H),
3.90 (singlet, 3H),
3.80 (singlet, 3H),
3.72 (singlet, 3H),
2.21 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),
1.80 (singlet, 3H)

Example 98

3-[2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)-benzyl]-benzoic acid

A procedure similar to that described in Example 96 above was followed, but using 3-[2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]benzoic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 56%.

$[\alpha]_D^{23}$ = +9 (C=0.2, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.40 (doublet of doublets, J=1.8, 7.1Hz, 1H),
7.31-7.23 (multiplet, 2H),
7.19 (singlet, 1H),
7.18 (doublet of doublets, J=1.8, 7.1Hz, 1H),
6.93 (singlet, 1H),
4.70 (doublet, J=9.6Hz, 1H),
4.18 (doublet, J=15.2Hz, 1H),
4.13 (doublet, J=15.2Hz, 1H),
4.08 (doublet, J=3.3Hz, 1H),
3.91 (triplet, J=9.6Hz, 1H),
3.83-3.73 (multiplet, 4H),
3.79 (singlet, 3H),
3.76 (singlet, 3H)

Example 99

2-[2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and methyl 2-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 43%.

$[\alpha]_D^{23}$ = -3.3 (C=0.88, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
7.87 (doublet of doublets, J=1.3, 7.5Hz, 1H),
7.38 (doublet of triplets, J=1.3, 7.5Hz, 1H),
7.26 (doublet of triplets, J=1.3, 7.5Hz, 1H),
7.11 (doublet of doublets, J=1.3, 7.5Hz, 1H),
6.94 (singlet, 1H),
6.55 (singlet, 1H),
5.52 (doublet, J=3.4Hz, 1H),
5.52 (triplet, J=10.0Hz, 1H),
5.21 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.90 (doublet, J=10.0Hz, 1H),
4.32 (singlet, 2H),
4.22-4.05 (multiplet, 3H),
3.83 (singlet, 3H),
3.79 (singlet, 3H),
3.70 (singlet, 3H),
2.21 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),
1.79 (singlet, 3H)

Example 100

Sodium 2-[2',5'-dimethoxy-4'-(β-D-galactopyranosyl)-benzyl]-benzoate

A procedure similar to that described in Example 96 above was followed, but using 2-[2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]benzoic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 39.3%.

$[\alpha]_D^{23}$ = +17 (C=0.25, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.40 (doublet of doublets, J=1.5, 7.2Hz, 1H),
7.32-7.24 (multiplet, 2H),

7.19 (singlet, 1H),
7.18 (doublet, J=7.2Hz, 1H),
6.93 (singlet, 1H),
4.70 (doublet, J=9.7Hz, 1H),
4.18 (doublet, J=15.3Hz, 1H),
4.13 (doublet, J=15.3Hz, 1H),
4.08 (doublet, J=3.0Hz, 1H),
3.92 (triplet, J=9.7Hz, 1H),
3.84-3.73 (multiplet, 4H),
3.79 (singlet, 3H),
3.76 (singlet, 3H)

Example 101

5-[2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-salicylic acid Ethyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and ethyl 5-(bromomethyl)acetylsalicylate to give the titled compound as a foam in a yield of 71.6%.

$[\alpha]_D^{23}$ = -3.3 (C=0.88, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:

7.86 (doublet, J=2.3Hz, 1H),
7.30 (doublet of doublets, J=2.3, 8.4Hz, 1H),
6.96 (doublet, J=8.4Hz, 1H),
6.94 (singlet, 1H),
6.61 (singlet, 1H),
5.52 (triplet, J=10.0Hz, 1H),
5.51 (doublet, J=3.5Hz, 1H),
5.20 (doublet of doublets, J=3.5, 10.0Hz, 1H),
4.90 (doublet, J=10.0Hz, 1H),
4.31 (qualtet, J=7.1Hz, 2H),
4.21-4.04 (multiplet, 3H),

4.01 (doublet, J=15.2Hz, 1H),
3.89 (doublet, J=15.2Hz, 1H),
3.79 (singlet, 3H),
3.72 (singlet, 3H),
2.31 (singlet, 3H),
2.20 (singlet, 3H),
2.02 (singlet, 3H),
1.98 (singlet, 3H),
1.79 (singlet, 3H),
1.35 (triplet, J=7.1Hz, 3H)

Example 102

5-[2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)benzyl]-salicylic acid

A procedure similar to that described in Example 96 above was followed, but using 5-[2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-salicylic acid ethyl ester to give the titled compound as a freeze-dried product in a yield of 55.2%.

$[\alpha]_D^{23}$ = +13 (C=0.24, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.69 (doublet, J=2.3Hz, 1H),
7.32 (doublet of doublets, J=2.3, 8.2Hz, 1H),
7.22 (singlet, 1H),
7.00 (singlet, 1H),
6.86 (doublet, J=8.2Hz, 1H),
4.71 (doublet, J=9.8Hz, 1H),
4.08 (doublet, J=3.1Hz, 1H),
3.94 (singlet, 1H),
3.93 (singlet, 1H),
3.92 (triplet, J=9.8Hz, 1H),
3.84-3.75 (multiplet, 4H),
3.80 (singlet, 3H),

3.79 (singlet, 3H)

Example 103

3-[2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-salicylic acid Ethyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and ethyl 3-(bromomethyl)acetylsalicylate to give the titled compound as a foam in a yield of 53.1%.

$[\alpha]_D^{23}$ = -4.7 (C=0.47, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.88 (doublet of doublets, J=1.9, 7.7Hz, 1H),
7.26 (doublet of doublets, J=1.9, 7.7Hz, 1H),
7.19 (triplet, J=7.7Hz, 1H),
6.96 (singlet, 1H),
6.51 (singlet, 1H),
5.53 (doublet, J=3.6Hz, 1H),
5.49 (triplet, J=9.9Hz, 1H),
5.21 (doublet of doublets, J=3.6, 9.9Hz, 1H),
4.91 (doublet, J=9.9Hz, 1H),
4.32 (qualtet, J=7.2Hz, 2H),
4.23-4.05 (multiplet, 3H),
3.90 (singlet, 2H),
3.80 (singlet, 3H),
3.68 (singlet, 3H),
2.29 (singlet, 3H),
2.21 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),
1.80 (singlet, 3H),
1.36 (triplet, J=7.2Hz, 3H)

Example 104

3-[2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)benzyl]-salicylic acid

A procedure similar to that described in Example 96 above was followed, but using 3-[2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-salicylic acid ethyl ester to give the titled compound as a freeze-dried product in yield of 87.4%.

$[\alpha]_D^{23}$ = +8.7 (C=0.23, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.73 (doublet of doublets, J=1.5, 7.7Hz, 1H),
7.24 (singlet, 1H),
7.22 (doublet of doublets, J=1.5, 7.7Hz, 1H),
6.88 (singlet, 1H),
6.88 (triplet, J=7.7Hz, 1H),
4.71 (doublet, J=9.8Hz, 1H),
4.09 (doublet, J=3.4Hz, 1H),
3.98 (singlet, 1H),
3.97 (singlet, 1H),
3.93 (triplet, J=9.8Hz, 1H),
3.83-3.73 (multiplet, 4H),
3.82 (singlet, 3H),
3.73 (singlet, 3H)

Example 105

4-[2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-benzyl]-benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and 4-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 66%.

$[\alpha]_D^{23}$ = +2.4 (C= 0.42, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
7.92 (doublet, J=8.1Hz, 2H),
7.24 (doublet, J=8.1Hz, 2H),
7.16 (singlet, 1H),
6.40 (singlet, 1H),
5.53 (triplet, J=10.1Hz, 1H),
5.49 (doublet, J=2.7Hz, 1H),
5.17 (doublet of doublets, J=2.7, 10.1Hz, 1H),
4.80 (doublet, J=10.1Hz, 1H),
4.16-3.92 (multiplet, 5H),
3.88 (singlet, 3H),
3.85 (singlet, 3H),
3.76 (singlet, 3H),
2.18 (singlet, 3H),
2.02(singlet, 3H),
1.98(singlet, 3H),
1.75(singlet, 3H)

Example 106

4-[2',4'-Dimethoxy-5'-(β-D-galactopyranosyl)benzyl]-benzoic acid

A procedure similar to that described in Example 96 above was followed, but using 4-[2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-benzoic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 63.3%.

$[\alpha]_D^{23}$ = +14 (C=0.14, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, $CDCl_3$) δ ppm:
7.77 (doublet, J=8.1Hz, 2H),
7.40 (singlet, 1H),
7.35 (doublet, J=8.1Hz, 2H),
6.75 (singlet, 1H),
4.65 (doublet, J=9.7Hz, 1H),

4.06 (doublet, J=3.1Hz, 1H),
3.99 (singlet, 2H)
3.96 (triplet, J=9.7Hz, 1H),
3.88 (singlet, 3H)
3.84 (singlet, 3H)
3.82-3.72 (multiplet, 4H)

Example 107

3-[2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 3-(bromomethyl)benzoate to give the titled compound as a freeze-dried product in a yield of 41.7%,

$[\alpha]_D^{23}$ = +3.9 (C=0.69, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
7.89 (singlet, 1H),
7.83 (doublet of triplets, J=1.8, 6.9Hz, 1H),
7.36-7.28 (multiplet, 2H),
7.15 (singlet, 1H),
6.41 (singlet, 1H),
5.54 (triplet, J=10.0Hz, 1H),
5.49 (doublet, J=3.2Hz, 1H),
5.16 (doublet of doublets, J=3.2, 10.0Hz, 1H),
4.78 (doublet, J=10.0Hz, 1H),
4.18-3.93 (multiplet, 5H),
3.90 (singlet, 3H),
3.85 (singlet, 3H),
3.78 (singlet, 3H),
2.19 (singlet, 3H),
2.03(singlet, 3H),
1.98(singlet, 3H),

1.74(singlet, 3H)

Example 108

3-[2',4'-Dimethoxy-5'-(β-D-galactopyranosyl)benzyl]-benzoic acid

A procedure similar to that described in Example 96 above was followed, but using 3-[2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-benzoic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 80.3%.

$[\alpha]_D^{23}$ = +23 (C=0.24, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.72 (singlet, 1H),
7.68 (doublet, J=7.6Hz, 1H),
7.41 (singlet, 1H),
7.39 (triplet, J=7.6Hz, 1H),
7.36 (doublet, J=7.6Hz, 1H),
6.75 (singlet, 1H),
4.65 (doublet, J=9.9Hz, 1H),
4.06 (doublet, J=3.2Hz, 1H),
4.01 (doublet, J=15.4Hz, 1H),
3.97 (doublet, J=15.4Hz, 1H),
3.97 (triplet, J=9.9Hz, 1H),
3.88 (singlet, 3H),
3.84 (singlet, 3H),
3.82-3.72 (multiplet, 3H),
3.75 (doublet of doublets, J=3.2, 9.9Hz, 1H)

Example 109

2-[2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-

acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 2-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 29.6%.

$[\alpha]_D^{23}$ = +10.0 (C=0.62, $CDCl_2$)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) ppm:

7.86 (doublet of doublets, J=1.3, 7.8Hz, 1H),
7.35 (doublet of triplets, J=1.3, 7.8Hz, 1H),
7.22 (doublet of triplets, J=1.3, 7.8Hz, 1H),
7.08 (singlet, 1H),
7.04 (doublet of doublets, J=1.3, 7.8Hz, 1H),
6.40 (singlet, 1H),
5.48 (triplet, J=10.0Hz, 1H),
5.47 (doublet, J=3.3Hz, 1H),
5.15 (doublet of doublets, J=3.3, 10.0Hz, 1H),
4.75 (doublet, J=10.0Hz, 1H),
4.35 (doublet, J=16.2Hz, 1H),
4.21 (doublet, J=16.2Hz, 1H),
4.16-3.92 (multiplet, 3H),
3.90 (singlet, 3H),
3.85 (singlet, 3H),
3.74 (singlet, 3H),
2.17 (singlet, 3H),
2.02 (singlet, 3H),
1.97 (singlet, 3H),
1.75 (singlet, 3H)

Example 110

Sodium 2-[2',4'-dimethoxy-5'-(β-D-galactopyranosyl)-benzyl]benzoate

A procedure similar to that described in Example 96 above was followed, but using 2-[2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-benzoic acid methyl ester

to give the titled compound as a freeze-dried product in a yield of 66.2%.

$[\alpha]_D^{23}$ = +9.2 (C= 0.13, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.36 (doublet of doublets, J=1.7, 7.1Hz, 1H),
7.30 (singlet, 1H),
7.28-7.21 (multiplet, 2H),
7.17 (doublet, J=7.1Hz, 1H),
6.71 (singlet, 1H),
4.62 (doublet, J=9.9Hz, 1H),
4.10 (doublet, J=15.2Hz, 1H),
4.06 (doublet, J=15.2Hz, 1H),
4.05 (doublet, J=3.6Hz, 1H),
3.98 (triplet, J=9.9Hz, 1H),
3.87 (singlet, 3H),
3.82 (singlet, 3H)
3.80-3.71 (multiplet, 4H)

Example 111

5-[2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acety -β-D-galactopyranosyl)benzyl]salicylic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 5-(bromomethyl)acetylsalicylate to give the titled compound as a foam in a yield of 34.6%.

$[\alpha]_D^{23}$ = +4.3 (C=0.70, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.86 (doublet, J=2.3Hz, 1H),
7.32 (doublet of doublets, J=2.3, 8.4Hz, 1H),
7.18 (singlet, 1H),
6.96 (triplet, J=8.4Hz, 1H),
6.40 (singlet, 1H),

5.54 (triplet, J=9.9Hz, 1H),
5.50 (doublet, J=3.5Hz, 1H),
5.17 (doublet of doublets, J=3.5, 9.9Hz, 1H),
4.80 (doublet, J=9.9Hz, 1H),
4.16-4.00 (multiplet, 3H),
3.94 (doublet, J=15.1Hz, 1H),
3.86 (doublet, J=15.1Hz, 1H),
3.85 (singlet, 6H),
3.78 (singlet, 3H),
2.32 (singlet, 3H),
2.20 (singlet, 3H),
2.03 (singlet, 3H),
1.98 (singlet, 3H),
1.74 (singlet, 3H)

Example 112

5-[2',4'-Dimethoxy-5'-(β-D-galactopyranosyl)benzyl]-salicylic acid

A procedure similar to that described in Example 96 above was followed, but using 5-[2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-salicylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 75.8%.

$[\alpha]_D^{23}$ = +16 (C=0.22, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.68 (doublet, J=2.1Hz, 1H),
7.36 (doublet of doublets, J=2.1, 8.5Hz, 1H),
7.35 (singlet, 1H),
6.87 (doublet, J=8.5Hz, 1H),
6.72 (singlet, 1H),
4.63 (doublet, J=9.9Hz, 1H),
4.05 (doublet, J=3.3Hz, 1H),
3.95 (triplet, J=9.9Hz, 1H),

3.88-3.71 (multiplet, 6H),
3.86 (singlet, 3H),
3.82 (singlet, 3H)

Example 113

4-[2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]salicylic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 4-(bromomethyl)acetylsalicylate to give the titled compound as a foam in a yield of 43.3%.

$[\alpha]_D^{23}$ = +4.1 (C=0.88, CH_3OH)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ PPM:
7.90 (doublet, J=8.1Hz, 1H),
7.19 (singlet, 1H),
7.11 (doublet of doublets, J=1.5, 8.1Hz, 1H),
6.89 (doublet, J=1.5Hz, 1H),
6.39 (singlet, 1H),
5.53 (triplet, J=10.1Hz, 1H),
5.50 (doublet, J=3.4Hz, 1H),
5.18 (doublet of doublets, J=3.4, 10.1Hz, 1H),
4.81 (doublet, J=10.1Hz, 1H),
4.19-4.01 (multiplet, 3H),
3.97 (doublet, J=15.3Hz, 1H),
3.87 (doublet, J=15.3Hz, 1H),
3.85 (singlet, 3H),
3.83 (singlet, 3H),
3.74 (singlet, 3H),
2.32 (singlet, 3H),
2.20 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),

1.76 (singlet, 3H)

Example 114

Sodium 5-[2',4'-dimethoxy-5'-(β-D-galactopyranosyl)-benzyl]salicylate

A procedure similar to that described in Example 96 above was followed, but using 4-[2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)benzyl]-salicylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 92.5%.

$[\alpha]_D^{23}$ = +16 (C=0.21, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:
7.70 (doublet, J=8.0Hz, 1H),
7.38 (singlet, 1H),
6.82 (doublet, J=8.0Hz, 1H),
6.78 (singlet, 1H),
6.75 (singlet, 1H),
4.78 (doublet, J=9.6Hz, 1H),
4.06 (doublet, J=3.2Hz, 1H),
3.96 (triplet, J=6.1Hz, 1H),
3.92 (singlet, 2H),
3.88 (singlet, 3H),
3.84 (singlet, 3H)
3.82-3.72 (multiplet, 4H)

Example 115

4-[2',5'-Dimethoxy-4'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-5-tri-n-butylstannyl benzene and methyl 4-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 83.3%.

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ PPM:
7.92 (doublet, J=8.2Hz, 2H),
7.22 (doublet, J=8.2Hz, 2H),
6.97 (singlet, 1H),
6.60 (singlet, 1H),
5.53 (triplet, J=10.0Hz, 1H),
5.37 (doublet, J=3.1Hz, 2H),
5.30 (singlet, 2H),
5.21 (doublet of doublets, J=3.5, 10.0Hz, 1H),
4.89 (doublet, J=10.0Hz, 1H),
3.97 (quartet, J=6.0Hz, 1H),
3.89 (singlet, 3H),
3.78 (singlet, 3H),
3.72 (singlet, 3H),
2.24 (singlet, 3H),
1.99 (singlet, 3H),
1.79 (singlet, 3H),
1.22(doublet, J=6.0Hz, 3H)

Example 116

4-(2',5'-Dimethoxy-4'-(β-L-fucopyranosyl)benzyl]benzoic acid

A procedure similar to that described in Example 96 above was followed, but using 4-[2',5'-dimethoxy-4'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]benzoic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 68.4%.

$[\alpha]_D^{23}$ = -4.9 (C= 0.47, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CD_3OD) δ ppm:
7.88 (doublet, J=8.2Hz, 2H),
7.30 (doublet, J=8.2Hz, 2H),
7.20 (singlet, 1H),
6.80 (singlet, 1H),

4.62 (doublet, J=9.8Hz, 1H),
4.00 (quartet, J=8.0Hz, 1H),
3.81-3.72 (multiplet, 2H),
3.78 (triplet, J=9.8Hz, 1H),
3.79 (singlet, 3H),
3.74 (singlet, 3H),
3.59 (doublet of doublets, J=3.5, 9.8Hz, 1H),
1.25 (doublet, J=6.5Hz, 3H)

Example 117

5-[2',5'-Dimethoxy-4'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]salicylic acid Ethyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-5-tri-n-butylstannyl benzene and ethyl 4-(bromomethyl)acetylsalicylate to give the titled compound as a foam in a yield of 45.7%.

$[\alpha]_D^{23}$ = +11.4 (C=0.72, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ PPM:
7.86 (doublet, J=2.4Hz, 1H),
7.29 (doublet, J=2.4Hz, 1H),
6.98 (singlet, 2H),
6.62 (singlet, 1H),
5.53 (triplet, J=9.9Hz, 1H),
5.37 (doublet, J=2.9Hz, 2H),
5.21 (doublet of doublets, J=2.9, 9.9Hz, 1H),
4.89 (doublet, J=9.9Hz, 1H),
4.32 (quartet, J=7.2Hz, 2H),
4.00 (doublet, J=15.2Hz, 1H),
3.97 (quartet, J=6.7Hz, 1H),
3.88 (doublet, J=15.2Hz, 1H),
3.80 (singlet, 3H),
3.74 (singlet, 3H),

2.33 (singlet, 3H),
2.24 (singlet, 3H),
1.99 (singlet, 3H),
1.79 (singlet, 3H),
1.36 (triplet, J=7.2Hz, 1H),
1.22(doublet, J=6.0Hz, 3H)

Example 118

5-[2',5'-Dimethoxy-4'-(β-L-fucopyranosyl)benzyl]-salicylic acid

A procedure similar to that described in Example 96 above was followed, but using 5-[2',5'-dimethoxy-4'-2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]salicylic acid ethyl ester to give the titled compound as a freeze-dried product in a yield of 76.2%.

$[\alpha]_D^{23}$ = -2.8 (C=0.47, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CH_2Cl_3) δ ppm:
7.70 (doublet, J=2.2Hz, 1H),
7.32 (doublet of doublets, J=2.2, 8.5Hz, 1H),
7.19 (singlet, 1H),
6.79 (doublet, J=8.5Hz, 1H),
6.78 (singlet, 1H),
4.62 (doublet, J=9.6Hz, 1H),
3.86 (quartet, J=6.9Hz, 1H),
3.81-3.72 (multiplet, 3H),
3.81 (singlet, 3H),
3.73 (singlet, 3H),
3.58 (doublet of doublets, J=3.1, 9.6Hz, 1H),
1.25 (doublet, J=6.5Hz, 3H)

Example 119

4-[2',4'-Dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-6-tri-n-butylstannyl benzene and methyl 4-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 65.6%.

$[\alpha]_D^{23}$ = +2.5 (C=0.52, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
7.92 (doublet, J=8.3Hz, 2H),
7.23 (doublet, J=8.3Hz, 2H),
7.19 (singlet, 1H),
6.40 (singlet, 1H),
5.52 (triplet, J=10.0Hz, 1H),
5.33 (doublet, J=3.0Hz, 1H),
5.17 (doublet of doublets, J=3.0, 10.0Hz, 1H),
4.78 (doublet, J=10.0Hz, 1H),
3.98 (doublet, J=15.2Hz, 1H),
3.90 (doublet, J=15.2Hz, 1H),
3.88 (singlet, 3H),
3.84 (singlet, 3H),
3.75 (singlet, 3H),
2.20 (singlet, 3H),
1.98 (singlet, 3H),
1.74 (singlet, 3H),
1.19 (doublet, J=6.5Hz, 3H)

Example 120

4-[2',4'-Dimethoxy-5'-(β-L-fucopyranosyl)benzyl]benzoic acid

A procedure similar to that described in Example 96 above was followed, but using 4-[2',4'-dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]benzoic acid methyl ester to

give the titled compound as a freeze-dried product in a yield of 77.6%.

$[\alpha]_D^{23}$ = -5.4 (C=0.48, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

7.86 (doublet, J=8.1Hz, 2H),
7.37 (singlet, 1H),
7.30 (doublet, J=8.1Hz, 2H),
6.59 (singlet, 1H),
4.57 (doublet, J=9.7Hz, 1H),
3.97 (doublet, J=14.8Hz, 1H),
3.93 (doublet, J=14.8Hz, 1H),
3.84 (singlet, 3H),
3.80 (singlet, 3H),
3.72 (quartet, J=6.8Hz, 1H),
3.70 (doublet, J=3.5Hz, 1H),
3.56 (doublet of doublets, J=3.5, 9.7Hz, 1H),
1.25 (doublet, J=6.8Hz, 3H)

Example 121

3-[2',4'-Dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]benzoic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-6-tri-n-butylstannyl benzene and methyl 3-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 34.4%.

$[\alpha]_D^{23}$ = +0.0 (C=0.57, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

8.0-7.3 (multiplet, 4H),
7.18 (singlet, 1H),
6.40 (singlet, 1H),
5.53 (triplet, J=10.0Hz, 1H),
5.33 (doublet, J=3.6Hz, 1H),

5.17 (doublet of doublets, J=3.6, 10.0Hz, 1H),
3.96-3.87 (multiplet, 3H),
3.89 (singlet, 3H),
3.84 (singlet, 3H),
3.77 (singlet, 3H),
2.21 (singlet, 3H),
1.98 (singlet, 3H),
1.73 (singlet, 3H),
1.19 (doublet, J=6.5Hz, 3H)

Example 122

3-[2',4'-Dimethoxy-5'-(β-L-fucopyranosyl)benzyl]benzoic acid

A procedure similar to that described in Example 96 above was followed, but using 3-[2',4'-dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]benzoic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 37.3%.

$[\alpha]_D^{23}$ = -6.8 (C=0.25, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CD_3Cl_2OD) δ ppm:

7.87 (singlet, 1H),
7.77 (doublet, J=7.7Hz, 1H),
7.44 (doublet, J=7.7Hz, 1H),
7.37 (singlet, 1H),
7.30 (triplet, J=7.7Hz, 1H),
6.60 (singlet, 1H),
4.56 (doublet, J=9.6Hz, 1H),
3.97 (doublet, J=14.7Hz, 1H),
3.92 (doublet, J=14.7Hz, 1H),
3.84 (singlet, 3H),
3.82 (singlet, 3H),
3.73 (quartet, J=6.5Hz, 1H),
3.71 (doublet, J=3.3Hz, 1H),
3.56 (doublet of doublets, J=3.3, 9.6Hz, 1H),

1.25 (doublet, J=6.5Hz, 3H)

Example 123

3-[2',4'-Dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]salicylic acid Ethyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-6-tri-n-butylstannyl benzene and ethyl 3-(bromomethyl)acetylsalicylate to give the titled compound as a foam in a yield of 39.2%.

$[\alpha]_D^{23}$ = -2.7 (C=0.55, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ PPM:

7.83 (doublet of doublets, J=1.8, 7.3Hz, 1H),
7.22-7.12 (multiplet, 3H),
6.38 (singlet, 1H),
5.44 (triplet, J=9.9Hz, 1H),
5.33 (doublet, J=3.4Hz, 1H),
5.17 (doublet of doublets, J=3.4, 9.9Hz, 1H),
4.77 (doublet, J=9.9Hz, 1H),
4.31 (quartet, J=7.3Hz, 2H),
3.92 (quartet, J=6.6Hz, 1H),
3.84 (singlet, 3H),
3.72 (singlet, 3H),
2.39 (singlet, 3H),
2.21 (singlet, 3H),
1.97 (singlet, 3H),
1.96 (singlet, 3H),
1.35 (triplet, J=7.3Hz, 3H),
1.19 (doublet, J=6.6Hz, 3H)

Example 124

3-[2',4'-Dimethoxy-5'-(β-L-fucopyranosyl)benzyl)-salicylic acid

A procedure similar to that described in Example 96 above was followed, but using 3-[2',4'-dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]salicylic acid ethyl ester to give the titled compound as a freeze-dried product in a yield of 84.0%.

$[\alpha]_D^{23}$ = -1.3 (C=0.38, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

7.66 (doublet of doublets, J=1.5, 8.0Hz, 1H),
7.33 (singlet, 1H),
7.11 (doublet of doublets, J=1.5, 8.0Hz, 1H),
6.70 (triplet, J=8.0Hz, 1H),
6.61 (singlet, 1H),
4.55 (doublet, J=9.9Hz, 1H),
3.89 (singlet, 2H),
3.85 (singlet, 3H),
3.80 (singlet, 3H),
3.72 (quartet, J=6.5Hz, 1H),
3.69 (doublet, J=3.4Hz, 1H),
3.56 (doublet of doublets, J=3.4, 9.6Hz, 1H),
1.23 (doublet, J=6.5Hz, 3H)

Example 125

3-[2',4'-Dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]phenylacetic acid Ethyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-6-tri-n-butylstannyl benzene and ethyl 3-(bromomethyl)phenylacetate to give the titled compound as a foam in a yield of 15.9%.

$[\alpha]_D^{23}$ = +0.6 (C=1.1, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.3-7.0 (multiplet, 4H),
7.19 (singlet, 1H),
6.40 (singlet, 1H),
5.54 (triplet, J=10.0Hz, 1H),
5.33 (doublet, J=3.3Hz, 1H),
5.17 (doublet of doublets, J=3.3, 10.0Hz, 1H),
4.76 (doublet, J=10.0Hz, 1H),
4.13 (quartet, J=7.3Hz, 2H),
4.0-3.8 (multiplet, 3H),
3.84 (singlet, 3H),
3.76 (singlet, 3H),
3.57 (singlet, 2H),
2.22 (singlet, 3H),
1.98 (singlet, 3H),
1.73 (singlet, 3H),
1.23 (triplet, J=7.1Hz, 3H),
1.19 (doublet, J=6.4Hz, 3H)

Example 126

3-[2',4'-Dimethoxy-5'-(5-L-fucopyranosyl)benzyl]-phenylacetic acid

A procedure similar to that described in Example 96 above was followed, but using 3-[2',4'-dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)benzyl]phenylacetic acid ethyl ester to give the titled compound as a freeze-dried product in a yield of 56.0%.

$[\alpha]_D^{23}$ = -16.3 (C=0.43, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CD_3OD) δ ppm:
7.27 (singlet, 1H),
7.20 (singlet, 1H),
7.13 (doublet, J=7.5Hz, 1H),
7.06-7.04 (multiplet, 2H),
6.58 (singlet, 1H),

4.55 (doublet, J=9.9Hz, 1H),
3.98 (doublet, J=14.0Hz, 1H),
3.91 (doublet, J=14.0Hz, 1H),
3.83 (singlet, 6H),
3.72 (quartet, J=6.5Hz, 1H),
3.71 (doublet, J=3.1Hz, 1H),
3.58 (doublet of doublets, J=3.1, 9.4Hz, 1H),
1.22 (doublet, J=6.5Hz, 3H)

Example 127

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-4-carboxylic acid Methyl ester

A suspended solution of 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene (149.1mg, 0.197mmol), methyl 4-bromobenzoate (128.5mg, 0.598mmol), tetrakis(triphenylphosphine)palladium (0) (22.2mg, 0.0192mmol), triphenylphosphine (15.0mg, 0.0572mmol), copper(I) bromide (12.5mg, 0.0873mmol) and a catalytic amount of 2,6-di-tert-butyl-p-cresol in dimethyl formamide was refluxed for 4 hours under a nitrogen atmosphere.

The resulting mixture was diluted with ethyl acetate and washed with a saturated aqueous solution of potassium fluoride, sodium bicarbonate and brine, dried over magnesium sulfate, then evaporated under reduced pressure.

A purification of the resulting residue by column chromatography with ethyl acetae / hexane (1 / 3) afforded 99.2mg of the titled compound in a yield of 83.6%.

$[\alpha]_D^{23}$ = -11.8 (C=0.77, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ PPM:
8.07 (doublet, J=8.4Hz, 2H),
8.37 (doublet, J=8.4Hz, 2H),
7.09 (singlet, 1H),
6.86 (singlet, 1H),

5.57 (triplet, J=10.1Hz, 1H),
5.55 (doublet, J=3.4Hz, 1H),
5.25 (doublet of doublets, J=3.4, 10.1Hz, 1H),
4.98 (doublet, J=10.1Hz, 1H),
4.21-4.08 (multiplet, 3H),
3.94 (singlet, 3H),
3.84 (singlet, 3H),
3.79 (singlet, 3H),
2.23 (singlet, 3H),
2.05 (singlet, 3H),
2.01 (singlet, 3H),
1.85 (singlet, 3H)

Example 128

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-4-carboxylic acid

To a methanol solution (3ml) of 2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-4-carboxylic acid methyl ester (135.2 mg, 0.224mmol) was added a few drops of 28% sodium methoxide methanol solution. After being stirred for 6 hours at room temperature, the whole reaction mixture was neutralized by adding a small amount of Amberlyst 15 (acidic ion-exchange resin). An insoluble material was filtered off through celite pad and the filtrate was concentrated under reduced pressure.

A purification of the resulting residue by PLC plate (silicagel 60) with ethyl acetae / methanol / water (15/ 3 / 1) afforded the deacetylated compound.

To the above product was added 3ml of 1N sodium hydroxide solution and stirred for 6 hours at room temperature. After being acidified by adding 1N solution of hydrochrolic acid, the whole reaction mixture was concentrated under reduced pressure.

A purification of the resulting residue by PLC plate (silicagel 60) with ethyl acetae / methanol / water (15 / 3 / 2) and lyophilization afforded 46.4mg of the titled compound in a yield of 49.3%.

$[\alpha]_D^{23}$ = +5.2 (C=0.23, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ PPM:
7.94 (doublet, J=8.4Hz, 2H),
7.62 (doublet, J=8.4Hz, 2H),
7.37 (singlet, 1H),
7.12 (singlet, 1H),
4.79 (doublet, J=9.6Hz, 1H),
4.11 (doublet, J=2.9HZ, 1H),
3.98 (triplet, J=9.6Hz, 1H),
3.89-3.76(multiplet, 4H),
3.86 (singlet, 3H),
3.83 (singlet, 3H)

Example 129

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-carboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and methyl 3-bromobenzoate to give the titled compound as a foam in a yield of 69.9%.

$[\alpha]_D^{23}$ = -9.9 (C=1.03, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
8.17 (singlet, 1H),
8.01 (doublet, J=7.9Hz, 1H),
7.73 (doublet, J=7.9Hz, 1H),
7.48 (triplet, J=7.9Hz, 1H),
7.08 (singlet, 1H),
6.86 (singlet, 1H),

5.58 (triplet, J=10.0Hz, 1H),
5.55 (doublet of doublets, J=3.4Hz, 1H),
5.25 (doublet of doublets, J=3.4, 10.0Hz, 1H),
4.98 (doublet, J=10.0Hz, 1H),
4.25-4.09 (multiplet, 3H),
3.94 (singlet, 3H),
3.85 (singlet, 3H),
3.79 (singlet, 3H),
2.23 (singlet, 3H),
2.05 (singlet, 3H),
2.01 (singlet, 3H),
1.85 (singlet, 3H)

Example 130

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-3-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 38.2%.

$[\alpha]_D^{23}$ = +8.1 (C=0.27, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:
8.01 (singlet, 1H),
7.88 (doublet, J=7.7Hz, 1H),
7.70 (doublet, J=7.7Hz, 1H),
7.50 (triplet, J=7.7Hz, 1H),
7.37 (singlet, 1H),
7.13 (singlet, 1H),
4.79 (doublet, J=9.8Hz, 1H),
4.11 (doublet, J=3.4Hz, 1H),
3.98 (triplet, J=9.8Hz, 1H),
3.89-3.77 (multiplet, 3H),

3.87 (singlet, 3H),
3.83 (singlet, 3H)
3.79 (doublet of doublets, J=3.4, 9.8Hz, 1H)

Example 131

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2-carboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and methyl 2-bromobenzoate to give the titled compound as a foam in a yield of 76.7%.

$[\alpha]_D^{23}$ = -6.0 (C=0.40, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
7.87 (doublet of doublets, J=1.2, 7.8Hz, 1H),
7.56 (doublet of triplets, J=1.2, 7.8Hz, 1H),
7.41 (doublet of triplets, J=1.2, 7.8Hz, 1H),
7.31 (doublet of doublets, J=1.2, 7.8Hz, 1H),
6.98 (singlet, 1H),
6.81 (singlet, 1H),
5.55 (doublet, J=3.4Hz, 1H),
5.54 (triplet, J=9.9Hz, 1H),
5.25 (doublet of doublets, J=3.4, 9.9Hz, 1H),
4.98 (doublet, J=9.9Hz, 1H),
4.32 (singlet, 2H),
4.25-4.08 (multiplet, 3H),
3.83 (singlet, 3H),
3.69 (singlet, 3H),
3.64 (singlet, 3H),
2.22 (singlet, 3H),
2.05 (singlet, 3H),
2.00 (singlet, 3H),
1.84 (singlet, 3H)

Example 132

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-2-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 23.0%.

$[\alpha]_D^{23}$ = +13 (C=0.16, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.58 (doublet of doublets, J=1.1, 7.5Hz, 1H),
7.51 (doublet of triplets, J=1.1, 7.5Hz, 1H),
7.44 (doublet of triplets, J=1.1, 7.5Hz, 1H),
7.38 (doublet of doublets, J=1.1, 7.5Hz, 1H),
7.24 (singlet, 1H),
7.05 (singlet, 1H),
4.77 (doublet, J=9.7Hz, 1H),
4.11 (doublet, J=3.4Hz, 1H),
3.97 (triplet, J=9.7Hz, 1H),
3.88-3.78 (multiplet, 4H),
3.85 (singlet, 3H),
3.75 (singlet, 3H)

Example 133

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-hydroxy-2-carboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and methyl 2-acetoxy-6-trifluoromethanesulfonyloxybenzoate to give the titled compound as a foam in a yield of 38.3%.

$[\alpha]_D^{23}$ = +0.3 (C=0.71, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm.

7.49 (triplet, J=8.0Hz, 1H),
7.23 (doublet, J=8.0Hz, 1H),
7.12 (doublet, J=8.0Hz, 1H),
6.99 (singlet, 1H),
6.79 (singlet, 1H),
5.54 (doublet, J=3.3Hz, 1H),
5.49 (triplet, J=10.0Hz, 1H),
5.24 (doublet of doublets, J=3.3, 10.0Hz, 1H),
4.96 (doublet, J=10.0Hz, 1H),
4.24-4.07 (multiplet, 3H),
3.81 (singlet, 3H),
3.70 (singlet, 3H),
3.55 (singlet, 3H),
2.30 (singlet, 3H),
2.22 (singlet, 3H),
2.05 (singlet, 3H),
1.99 (singlet, 3H),
1.82 (singlet, 3H)

Example 134

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-3-hydroxy-2-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',5'-dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-hydroxy-2-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 49.8%.

$[\alpha]_D^{23}$ = +4 (C=0.15, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.46 (triplet, J=7.9Hz, 1H),
7.23 (singlet, 1H),

7.02 (singlet, 1H),
7.02 (doublet, J=7.9Hz, 1H),
6.92 (doublet, J=7.9Hz, 1H),
4.76 (doublet, J=9.6HZ, 1H),
4.09 (doublet, J=3.2Hz, 1H),
3.94 (triplet, J=9.6Hz, 1H),
3.86-3.71 (multiplet, 4H),
3.83 (singlet, 3H),
3.74 (singlet, 3H)

Example 135

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2, 4-dicarboxylic acid Dimethyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and dimethyl 4-bromoisophtalate to give the titled compound as a foam in a yield of 89.9%.

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
8.52 (doublet, J=1.6Hz, 1H),
8.19 (doublet of doublets, J=1.6, 8.1Hz, 1H),
7.40 (doublet, J=8.1Hz, 1H),
6.99 (singlet, 1H),
6.81 (singlet, 1H),
5.55 (doublet, J=3.6Hz, 1H),
5.53 (triplet, J=9.9Hz, 1H),
5.25 (doublet of doublets, J=3.6, 9.9Hz, 1H),
4.98 (doublet, J=9.9Hz, 1H),
4.25-4.08 (multiplet, 3H),
3.96 (singlet, 3H),
3.84 (singlet, 3H),
3.70 (singlet, 3H),
3.68 (singlet, 3H),

2.22 (singlet, 3H),
2.05 (singlet, 3H),
2.00 (singlet, 3H),
1.84 (singlet, 3H)

Example 136

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-2,4-dicarboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',5'-dimethoxy-2'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2,4-dicarboxylic acid dimethyl ester to give the titled compound as a freeze-dried product in a yield of 99.1%.

$[\alpha]_D^{23}$ = +4.2 (C=0.15, H_2O)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:
8.00 (doublet, J=2.0Hz, 1H),
7.92 (doublet of doublets, J=2.0, 8.0Hz, 1H),
7.43 (doublet, J=8.0Hz, 1H),
7.25 (singlet, 1H),
7.07 (singlet, 1H),
4.78 (doublet, J=9.6Hz, 1H),
4.11 (doublet, J=3.1Hz, 1H),
3.89-3.76 (multiplet, 4H),
3.86 (singlet, 3H),
3.76 (singlet, 3H)

Example 137

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2-methylcarboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and

methyl 4-bromophenylacetate to give the titled compound as a foam in a yield of 51.4%.

$[\alpha]_D^{23}$ = -4.4 (C=0.48, CH_2Cl_2)

Nuclear Magentic Resonance spectrum (270MHz, $CDCl_3$ at 50°C) δ ppm:

7.43-7.07 (multiplet, 4H),
7.03 (singlet, 1H),
6.73 (singlet, 1H),
5.56 (triplet, J=9.9Hz, 1H),
5.54 (doublet, J=3.4Hz, 1H),
5.25 (doublet of doublets, J=3.4, 9.9Hz, 1H),
4.96 (doublet, J=9.9Hz, 1H),
4.23-4.08 (multiplet, 3H),
3.78 (singlet, 3H),
3.68 (singlet, 3H),
3.58 (singlet, 3H),
3.47 (singlet, 2H),
2.20 (singlet, 3H),
2.04 (singlet, 3H),
1.99 (singlet, 3H),
1.82 (singlet, 3H)

Example 138

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-2-methylcarboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',5'-dimethoxy-2'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2-methylcarboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 57.7%.

$[\alpha]_D^{23}$ = +6.0 (C=0.20, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.47-7.39 (multiplet, 3H),

7.29 (singlet, 2H),
6.90 (singlet, 1H),
4.78 (doublet, J=9.6Hz, 1H),
4.10 (doublet, J=3.2Hz, 1H),
3.96 (triplet, J=9.6Hz, 1H),
3.87-3.75 (multiplet, 4H),
3.79 (singlet, 3H),
3.72 (singlet, 3H),
3.50 (doublet, J=4.4Hz, 2H)

Example 139

2',5'-Dimethoxy-4'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-methylcarboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-5-tri-n-butylstannyl benzene and methyl 3-bromophenylacetate to give the titled compound as a foam in a yield of 47.9%.

$[\alpha]_D^{23}$ = -10 (C=0.79, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ PPM:

7.70-7.26 (multiplet, 4H),
7.06 (singlet, 1H),
6.85 (singlet, 1H),
5.55 (triplet, J=10.0HZ, 1H),
5.54 (doublet, J=3.5Hz, 1H),
5.24 (doublet of doublets, J=3.5, 10.0Hz, 1H),
4.98 (doublet, J=10.0Hz, 1H),
4.25-4.08 (multiplet, 3H),
3.83 (singlet, 3H),
3.78 (singlet, 3H),
3.71 (singlet, 3H),
3.68 (singlet, 2H),
2.23 (singlet, 3H),

2.05 (singlet, 3H),
2.01 (singlet, 3H),
1.85 (singlet, 3H)

Example 140

2',5'-Dimethoxy-4'-(β-D-galactopyranosyl)biphenyl-3-methylcarboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',5'-dimethoxy-2'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-methylcarboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 57.2%.

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ PPM:
7.48-7.43 (multiplet, 3H),
7.35 (singlet, 1H),
7.33-7.31 (multiplet, 1H),
7.11 (singlet, 1H),
4.79 (doublet, J=9.6Hz, 1H),
4.12 (doublet, J=3.3Hz, 1H),
3.98 (triplet, J=9.6Hz, 1H),
3.88-3.76 (multiplet, 4H),
3.86 (singlet, 3H),
3.82 (singlet, 3H),
3.60 (singlet, 2H)

Example 141

2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-4-carboxylic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 4-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 71.8%.

$[\alpha]_D^{23}$ = -42 (C=0.47, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
8.06 (doublet, J=8.4Hz, 2H),
7.58 (doublet, J=8.4Hz, 2H),
7.41 (singlet, 1H),
6.50 (singlet, 1H),
5.57 (triplet, J=10.0Hz, 1H),
5.51 (doublet, J=3.3Hz, 1H),
5.21 (doublet of doublets, J=3.3, 10.0Hz, 1H),
4.88 (doublet, J=10.0Hz, 1H),
4.18-4.03 (multiplet, 3H),
3.93 (singlet, 3H),
3.92 (singlet, 3H),
3.83 (singlet, 3H),
2.18 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),
1.82 (singlet, 3H)

Example 142

2',4'-Dimethoxy-5'-(β-D-galactopyranosyl)biphenyl-4-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-4-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 64.4%.

$[\alpha]_D^{23}$ = +33 (C=0.10, CH_3OH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:
8.02 (doublet, J=8.6Hz, 2H),
7.66 (doublet, J=8.6Hz, 2H),
7.54 (singlet, 1H),
6.82 (singlet, 1H),

4.71 (doublet, J=9.9Hz, 1H),
4.06 (doublet, J=3.0Hz, 1H),
3.97 (triplet, J=9.9Hz, 1H),
3.94 (singlet, 3H),
3.88 (singlet, 3H),
3.82 (triplet, J=6.1Hz, 1H),
3.77 (doublet of doublets, J=3.0, 9.9Hz, 1H),
3.73 (doublet, J=6.1Hz, 1H)

Example 143

2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-carboxylic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 3-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 41.5%.

$[\alpha]_D^{23}$ = -20.2 (C=0.87, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:
8.18 (singlet, 1H),
7.97 (doublet, J=7.9Hz, 1H),
7.68 (doublet, J=7.9Hz, 1H),
7.47 (triplet, J=7.9Hz, 1H),
7.38 (singlet, 1H),
6.51 (singlet, 1H),
5.59 (triplet, J=10.0Hz, 1H),
5.51 (doublet, J=3.3Hz, 1H),
5.21 (doublet of doublets, J=3.3, 10.0Hz, 1H),
4.86 (doublet, J=10.0Hz, 1H),
4.20-4.02 (multiplet, 5H),
3.93 (singlet, 3H),
3.92 (singlet, 3H),
3.83 (singlet, 3H),

2.19 (singlet, 3H),
2.03 (singlet, 3H),
1.99 (singlet, 3H),
1.83 (singlet, 3H)

Example 144

Sodium 2',4'-dimethoxy-5'-(β-D-galactopyranosyl)biphenyl-3-carboxylate

A procedure similar to that described in Example 128 above was followed, but using 2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-3-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 92.6%.

$[\alpha]_D^{23}$ = +23 (C=0.15, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ PPM:
7.99 (singlet, 1H),
7.84 (doublet, J=7.9Hz, 1H),
7.67 (doublet, J=7.9Hz, 1H),
7.53 (triplet, J=7.9Hz, 1H),
7.52 (singlet, 1H),
6.86 (singlet, 1H),
4.72 (doublet, J=9.8Hz, 1H),
4.07 (doublet, J=3.3Hz, 1H),
4.01 (triplet, J=9.8Hz, 1H),
3.96 (singlet, 3H),
3.90 (singlet, 3H),
3.84 (triplet, J=6.1Hz, 1H),
3.78 (doublet of doublets, J=3.3, 9.8Hz, 1H),
3.74 (doublet, J=6.1Hz, 2H)

Example 145

2',4'-Dimethoxy-5'-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)biphenyl-2-carboxylic acid Methyl ester

A procedure similar to that described in Example 95 above was followed, but using 1,3-dimethoxy-4-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-6-tri-n-butylstannyl benzene and methyl 2-(bromomethyl)benzoate to give the titled compound as a foam in a yield of 71.6%.

$[\alpha]_D^{23}$= +17 (C=0.35, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.84 (doublet, J=7.5Hz, 1H),
7.55 (triplet, J=7.5Hz, 1H),
7.37 (triplet, J=7.5Hz, 1H),
7.33-7.26 (multiplet, 2H),
6.42 (singlet, 1H),
5.56 (triplet, J=10.1Hz, 1H),
5.51 (doublet, J=3.2Hz, 1H),
5.20 (doublet of doublets, J=3.2, 10.1Hz, 1H),
4.85 (doublet, J=10.1Hz, 1H),
4.17-4.05 (multiplet, 3H),
3.91 (singlet, 3H),
3.72 (singlet, 3H),
3.67 (singlet, 3H),
2.17 (singlet, 3H),
2.03 (singlet, 3H),
1.98 (singlet, 3H),
1.82 (singlet, 3H)

Example 146

2',4'-Dimethoxy-5'-(β-D-galactopyranosyl)biphenyl-2-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',4'-dimethoxy-5'-(2,3,4,6-tetra-O-

acetyl-β-D-galactopyranosyl)biphenyl-2-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 73.1%.

$[\alpha]_D^{23}$ = -23 (C=0.50, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, D_2O) δ ppm:

7.76 (doublet, J=7.5Hz, 1H),
7.64 (triplet, J=7.5Hz, 1H),
7.48 (singlet, 1H),
7.47 (triplet, J=7.5Hz, 1H),
7.43 (triplet, J=7.5Hz, 1H),
6.75 (singlet, 1H),
4.72 (doublet, J=9.9Hz, 1H),
4.06 (doublet, J=3.3Hz, 1H),
3.99 (triplet, J=9.9Hz, 1H),
3.93 (singlet, 3H),
3.84-3.73 (multiolet, 4H),
3.79 (singlet, 3H)

Example 147

2',4'-Dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl) biphenyl-3-carboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-5-tri-n-butylstannyl benzene and methyl 3-bromobenzoate to give the titled compound as a foam in a yield of 59.7%.

$[\alpha]_D^{23}$ = +22.3 (C=0.73, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

8.16 (singlet, 1H),
8.00 (doublet, J=7.8Hz, 1H),
7.72 (doublet, J=7.8Hz, 1H),
7.47 (triplet, J=7.8Hz, 1H),
7.11 (singlet, 1H),

6.85 (singlet, 1H),
5.58 (triplet, J=10.0Hz, 1H),
5.39 (doublet, J=3.0Hz, 1H),
5.25 (doublet of doublets, J=3.0, 10.0Hz, 1H),
4.96 (doublet, J=10.0Hz, 1H),
4.01 (doublet, J=6.5Hz, 1H),
3.94 (singlet, 3H),
3.84 (singlet, 3H),
3.79 (singlet, 3H),
2.25 (singlet, 3H),
2.05 (singlet, 3H),
1.84 (singlet, 3H),
1.25 (doublet, J=6.5Hz, 3H)

Example 148

2' , 4'-Dimethoxy-5'-(β-L-fucopyranosyl) biphenyl-3-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',4'-dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-3-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 60.2%.

$[\alpha]_D^{23}$ = -4.0 (C=0.40, MeOH)

Nuclear Magentic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

8.15 (singlet, 1H),
7.96 (doublet, J=7.6Hz, 1H),
7.73 (doublet, J=7.6Hz, 1H),
7.49 (triplet, J=7.6Hz, 1H),
7.35 (singlet, 1H),
6.93 (singlet, 1H),
4.70 (doublet, J=9.7Hz, 1H),
3.76 (doublet, J=2.5Hz, 1H),
3.83(singlet, 1H),

3.81 (singlet, 1H),
3.63 (doublet of doublets, J=3.2, 9.7Hz, 1H),
1.29 (doublet, J=6.5Hz, 6H)

Example 149

2',4'-Dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-2-carboxylic acid Methyl ester

A procedure similar to that described in Example 127 above was followed, but using 1,4-dimethoxy-2-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)-5-tri-n-butylstannyl benzene and methyl 2-bromobenzoate to give the titled compound as a foam in a yield of 14.9%.

$[\alpha]_D^{23}$ = +18.9 (C=0.56, CH_2Cl_2)

Nuclear Magentic Resonance Spectrum (270MHz, $CDCl_3$) δ ppm:

7.86 (doublet, J=7.8Hz, 1H),
7.54 (triplet, J=7.8Hz, 1H),
7.51 (triplet, J=7.8Hz, 1H),
7.28 (doublet, J=7.8Hz, 1H),
7.00 (singlet, 1H),
6.80 (singlet, 1H),
5.54 (triplet, J=10.0Hz, 1H),
5.39 (doublet, J=3.2Hz, 1H),
5.25 (doublet of doublets, J=3.2, 10.0Hz, 1H),
4.96 (doublet, J=10.0Hz, 1H),
4.01 (quartet, J=6.5Hz, 1H),
3.83 (singlet, 3H),
3.70 (singlet, 3H),
3.63 (singlet, 3H),
2.25 (singlet, 3H),
2.00 (singlet, 3H),
1.83 (singlet, 3H),
1.24 (doublet, J=6.5Hz, 3H)

Example 150

2',4'-Dimethoxy-5'-(β-L-fucopyranosyl)biphenyl-2-carboxylic acid

A procedure similar to that described in Example 128 above was followed, but using 2',4'-dimethoxy-5'-(2,3,4-tri-O-acetyl-β-L-fucopyranosyl)biphenyl-2-carboxylic acid methyl ester to give the titled compound as a freeze-dried product in a yield of 76.2%.

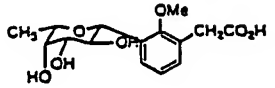
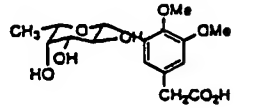
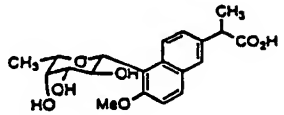
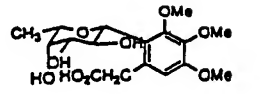
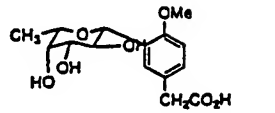
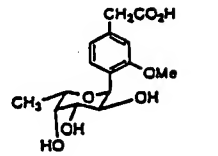
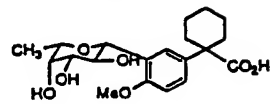
$[\alpha]_D^{23}$ = -13.2 (C=0.28, MeOH)

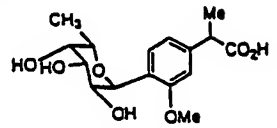
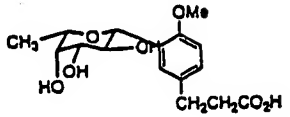
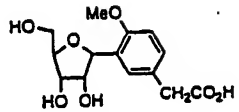
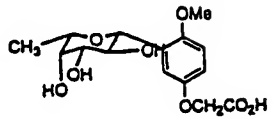
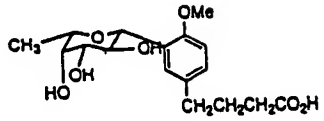
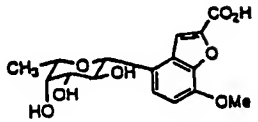
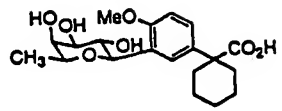
Nuclear Magentic Resonance Spectrum (400MHz, CD_3OD) δ ppm:

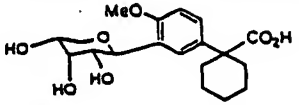
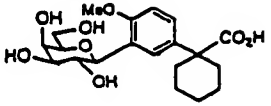
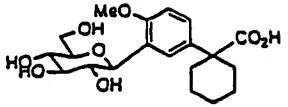
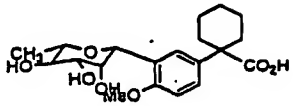
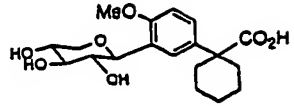
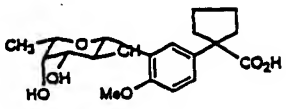
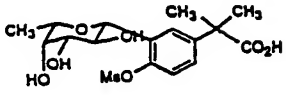
7.82 (doublet, J=7.9Hz, 1H),
7.55 (triplet, J=7.9Hz, 1H),
7.40 (triplet, J=7.9Hz, 1H),
7.32 (doublet, J=7.9Hz, 1H),
7.22 (singlet, 1H),
6.86 (singlet, 1H),
4.67 (doublet, J=9.6Hz, 1H),
3.82 (triplet, J=9.6Hz, 1H),
3.81 (singlet, 1H),
3.77 (quartet, J=6.5Hz, 3H)
3.75 (doublet, J=3.4Hz, 1H),
3.71 (singlet, 1H),
3.63 (doublet of doublets, J=3.4, 9.6Hz, 1H),
1.28 (doublet, J=6.5Hz, 6H)

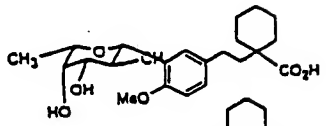
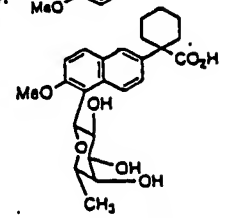
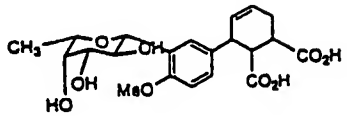
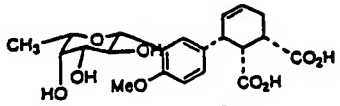
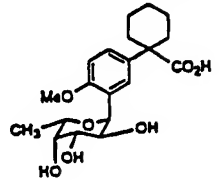
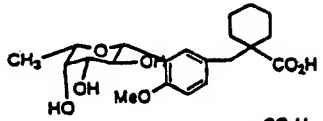
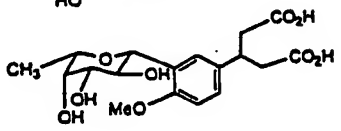
Structures of Compounds

Structures of some of the compounds set forth in the Examples are listed in the following table.

Example No.	Structure	Formula M.W.
1(b)		$C_{15}H_{20}O_7$ 312.32
2(b)		$C_{16}H_{22}O_8$ 342.34
3		$C_{20}H_{24}O_7$ 376.41
4		$C_{17}H_{24}O_9$ 372.37
5		$C_{15}H_{20}O_7$ 312.32
6		$C_{15}H_{20}O_7$ 312.32
7		$C_{20}H_{28}O_7$ 380.44

Example No.	Structure	Formula M.W.
8		$C_{16}H_{22}O_7$ 326.35
9		$C_{16}H_{22}O_7$ 326.35
10		$C_{14}H_{18}O_7$ 298.29
11		$C_{15}H_{20}O_8$ 328.32
12		$C_{17}H_{24}O_7$ 340.37
13		$C_{16}H_{18}O_8$ 338.31
14		$C_{20}H_{28}O_7$ 380.44

Example No.	Structure	Formula M.W.
15		$C_{19}H_{26}O_7$ 366.41
16		$C_{20}H_{28}O_8$ 396.44
17		$C_{20}H_{28}O_8$ 396.44
18		$C_{20}H_{28}O_7$ 380.44
19		$C_{19}H_{26}O_7$ 366.41
20		$C_{19}H_{26}O_7$ 366.41
21		$C_{17}H_{24}O_7$ 340.37

Example No.	Structure	Formula M.W.
22		$C_{12}H_{32}O_7$ 408.49
23		$C_{24}H_{30}O_7$ 430.50
24		$C_{21}H_{26}O_9$ 422.43
25		$C_{21}H_{26}O_9$ 422.43
26		$C_{20}H_{28}O_7$ 380.44
27		$C_{21}H_{30}O_7$ 394.46
28		$C_{18}H_{24}O_9$ 384.38

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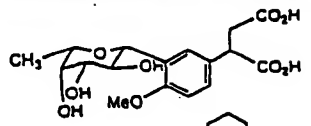
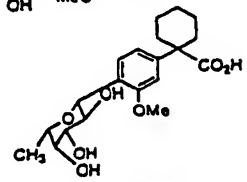
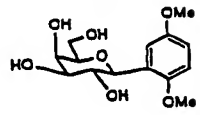
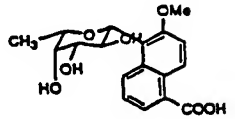
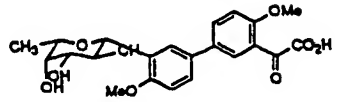
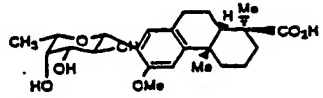
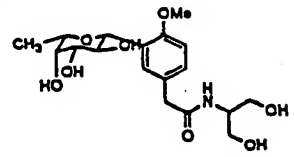
Example No.	Structure	Formula M.W.
29		$C_{17}H_{22}O_9$ 370.36
30		$C_{20}H_{28}O_7$ 380.44
31		$C_{14}H_{20}O_7$ 300.31
32		$C_{18}H_{20}O_7$ 348.35
33		$C_{22}H_{24}O_9$ 432.43
34		$C_{24}H_{34}O_7$ 434.53
35		$C_{18}H_{27}NO_8$ 385.41

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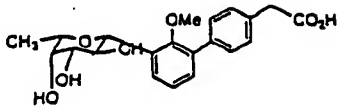
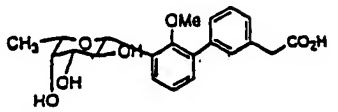
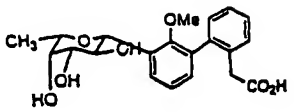
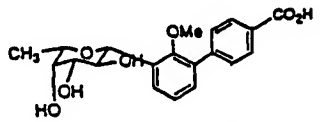
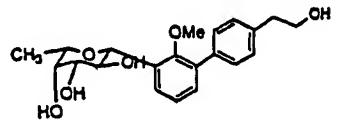
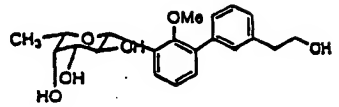
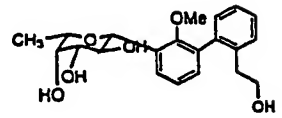
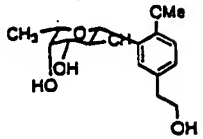
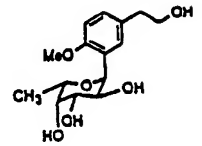
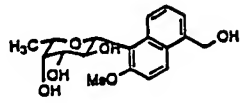
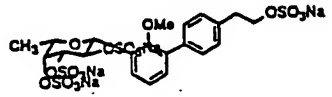
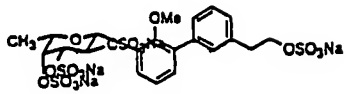
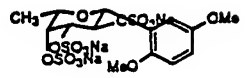
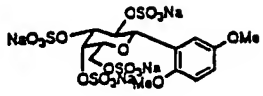
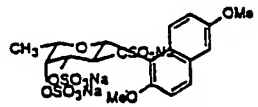
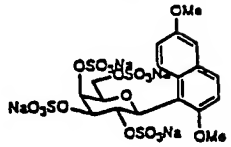
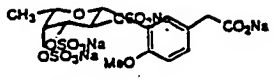
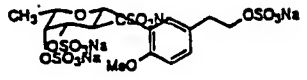
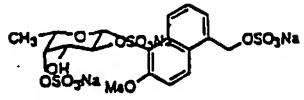
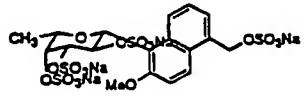
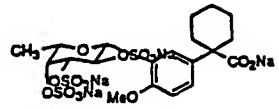
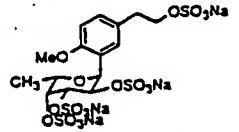
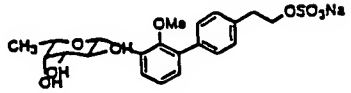
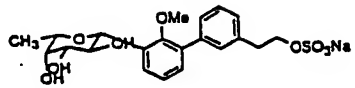
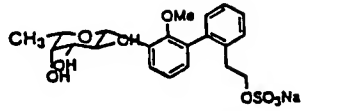
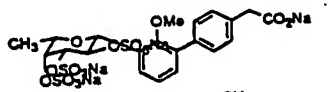
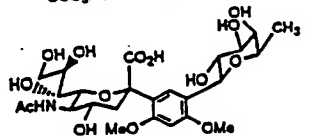
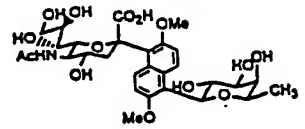
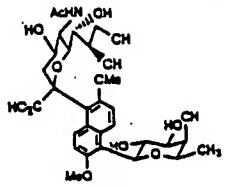
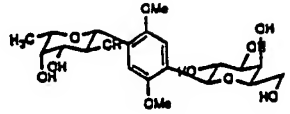
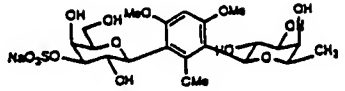
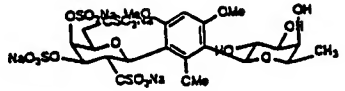
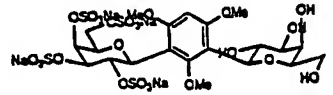
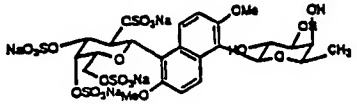
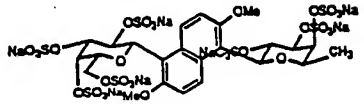
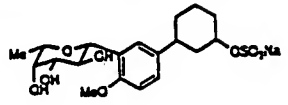
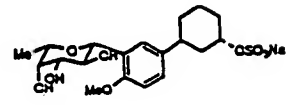
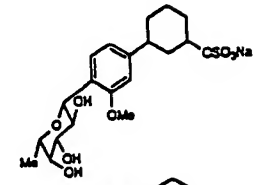
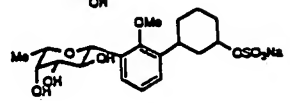
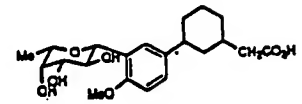
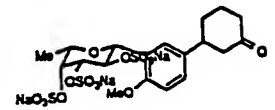
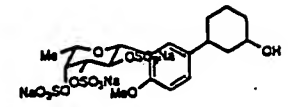
Example No.	Structure	Formula M.W.
36(c)		$C_{21}H_{24}O_7$ 388.42
37(c)		$C_{21}H_{24}O_7$ 388.42
38(c)		$C_{21}H_{24}O_7$ 388.42
39(c)		$C_{20}H_{22}O_7$ 374.39
40		$C_{21}H_{26}O_6$ 374.43
41		$C_{21}H_{26}O_6$ 374.43
42		$C_{21}H_{26}O_6$ 374.43

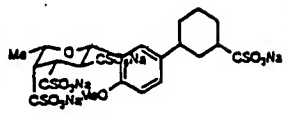
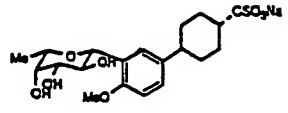
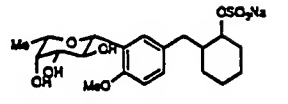
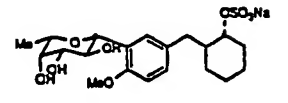
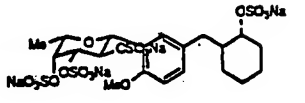
Example No.	Structure	Formula M.W.
43		$C_{15}H_{22}O_6$ 298.34
44		$C_{15}H_{22}O_6$ 298.34
45		$C_{18}H_{22}O_6$ 334.37
46		$C_{21}H_{22}Na_4O_{18}S_4$ 782.59
47		$C_{21}H_{22}Na_4O_{18}S_4$ 782.59
48		$C_{14}H_{17}Na_3O_{13}S_3$ 590.43
49		$C_{14}H_{16}Na_4O_{19}S_4$ 708.47

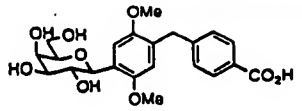
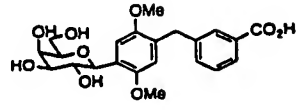
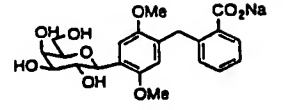
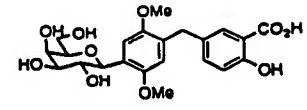
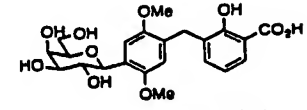
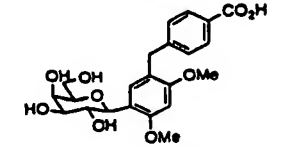
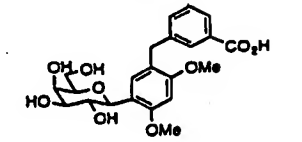
Example No.	Structure	Formula M.W.
50		$C_{18}H_{19}Na_3O_{15}S_3$ 640.49
51		$C_{18}H_{18}Na_4O_{19}S_4$ 758.53
52		$C_{15}H_{16}Na_4O_{16}S_3$ 640.42
53		$C_{15}H_{18}Na_4O_{18}S_4$ 706.50
54		$C_{18}H_{19}Na_3O_{15}S_3$ 640.49
55		$C_{18}H_{18}Na_4O_{18}S_4$ 742.53
56		$C_{20}H_{24}Na_4O_{16}S_3$ 708.54

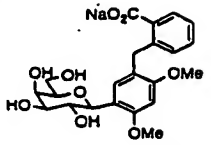
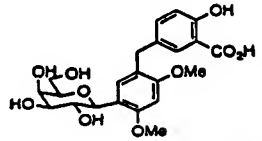
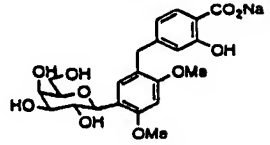
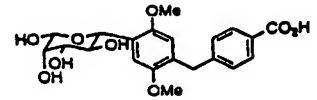
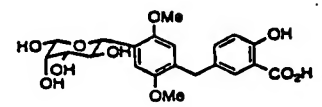
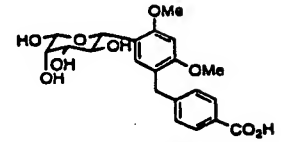
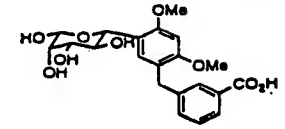
Example No.	Structure	Formula M.W.
57		$C_{13}H_{18}Na_4O_{18}S_4$ 706.50
58		$C_{21}H_{25}NaO_9S$ 476.47
59		$C_{21}H_{25}NaO_9S$ 476.47
60		$C_{21}H_{25}NaO_9S$ 476.47
61		$C_{21}H_{20}Na_4O_{16}S$ 716.52
62(c)		$C_{25}H_{37}NO_{14}$ 575.57
63		$C_{29}H_{39}NO_{14}$ 625.63

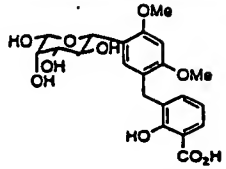
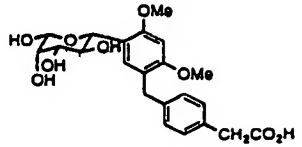
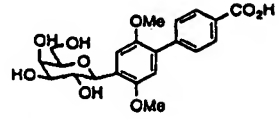
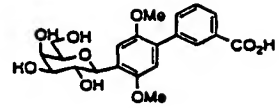
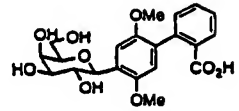
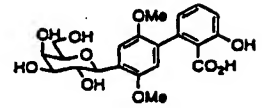
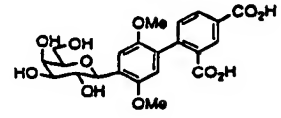
Example No.	Structure	Formula M.W.
64		$C_{39}H_{39}NO_{14}$ 625.63
65		$C_{20}H_{30}O_{11}$ 446.45
67(d)		$C_{21}H_{31}NaO_{15}S$ 578.52
68		$C_{21}H_{28}Na_4O_{24}S_4$ 884.64
69		$C_{21}H_{28}Na_4O_{23}S_4$ 900.64
70		$C_{24}H_{28}Na_4O_{23}S_4$ 904.67
71		$C_{24}H_{25}Na_7O_{22}S_7$ 1210.79

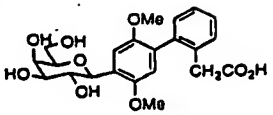
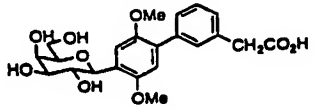
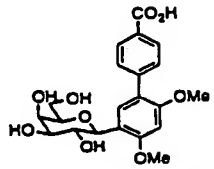
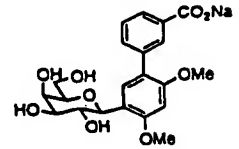
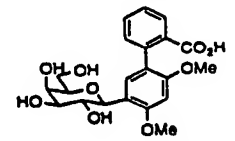
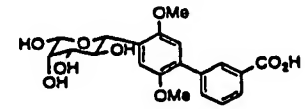
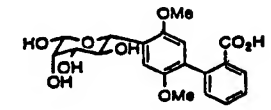
Example No.	Structure	Formula M.W.
72 (g)		$C_{19}H_{17}NaO_9S$ 454.47
73(d)		$C_{19}H_{17}NaO_9S$ 454.47
74(e)		$C_{19}H_{17}NaO_9S$ 454.47
75(e)		$C_{19}H_{17}NaO_9S$ 454.47
76(c)		$C_{21}H_{30}O_7$ 394.46
77(b)		$C_{19}H_{23}Na_3O_{13}S_3$ 656.53
77(c)		$C_{19}H_{25}Na_3O_{13}S_3$ 658.55

Example No.	Structure	Formula M.W.
78(b)		$C_{19}H_{14}Na_4O_{18}S_4$ 760.59
79(g)		$C_{19}H_{27}NaO_9S$ 454.47
80(d)		$C_{20}H_{29}NaO_9S$ 468.49
81(b)		$C_{20}H_{29}NaO_9S$ 468.49
82(c)		$C_{20}H_{26}Na_4O_{18}S_4$ 774.61

Example No.	Structure	Formula M.W.
96		$C_{22}H_{26}O_9$ 434.4420
98		$C_{22}H_{26}O_9$ 434.4420
100		$C_{22}H_{25}NaO_9$ 456.4239
102		$C_{22}H_{26}O_{10}$ 450.4414
104		$C_{22}H_{26}O_{10}$ 450.4414
106		$C_{22}H_{26}O_9$ 434.4420
108		$C_{22}H_{26}O_9$ 434.4420

Example No.	Structure	Formula M.W.
110		$C_{22}H_{25}NaO_9$ 456.4239
112		$C_{22}H_{26}O_{10}$ 450.4414
114		$C_{22}H_{25}NaO_{10}$ 472.4233
116		$C_{21}H_{24}O_9$ 420.4152
118		$C_{21}H_{24}O_{10}$ 436.4146
120		$C_{21}H_{24}O_9$ 420.4152
122		$C_{21}H_{24}O_9$ 420.4152

Example No.	Structure	Formula M.W.
124		$C_{21}H_{24}O_{10}$ 436.4146
126		$C_{22}H_{26}O_9$ 434.4420
128		$C_{21}H_{24}O_9$ 420.4152
130		$C_{21}H_{24}O_9$ 420.4152
132		$C_{21}H_{24}O_9$ 420.4152
134		$C_{21}H_{24}O_{10}$ 436.4146
136		$C_{22}H_{24}O_{11}$ 464.4250

Example No.	Structure	Formula M.W.
138		$C_{22}H_{26}O_9$ 434.4420
140		$C_{22}H_{26}O_9$ 434.4420
142		$C_{21}H_{24}O_9$ 420.4152
144		$C_{21}H_{23}NaO_9$ 442.3971
146		$C_{21}H_{24}O_9$ 420.4152
148		$C_{20}H_{22}O_9$ 406.3884
150		$C_{20}H_{22}O_9$ 406.3884

Example A

Cloning of FT-VII Gene and Expression in CHO Cells

HL60 mRNA was purified using an mRNA Separation Kit (Clontech Laboratories, Inc., Palo Alto, CA, USA). Human FT-VII cDNA was obtained from this HL60 mRNA by the RT-PCR method using an mRNA PCR Kit (Takara, 4-1, 3-chome, Seta, Ohtsu-shi, 520-21 Japan).

First, the cDNA was synthesized with a random primer from the mRNA after which fucosyltransferase type VII cDNA was amplified from this HL60 cDNA (synthesized from HL60 Poly A$^+$RNA by conventional means) using a specific primer of fucosyl-transferase type VII (sense primer: GTGGATGAATGCTGGGCACGG (SEQ. ID NO: 1), anti-sense primer: GATCTCAGGCCTGAAACCAACCCT (SEQ. ID NO: 2)). The PCR reaction was performed for 35 cycles using the method reported in Sasaki et al., J. Biol. Chem., (1994), 269, 14730-14737.

The amplified fucosyltransferase type VII cDNA was inserted into the KpnI, PstI site of expression vector pcDL-Sra296 (Takebe et al., Mol. Cel. Biol., (1988), 8, 466-472) to obtain pFT7R. The pFT7R and DHFR genes were co-transfected into CHO cells using the calcium phosphate method (Takahashi et al., Biochem. J., (1995), 311, 657-665) and were additionally analyzed using transfectant colonies grown on nucleic acid-free MEM medium containing 10% fetal bovine serum that had been sufficiently dialyzed with PBS.

A fucosyltransferase type VII expression strain was obtained from the resulting transfectant by fluorescent antibody staining using anti-sLe^x antibody CSLEX-1 (Fukushima et al., Cancer Res., (1984), 44, 5279-5285). Namely, after the resulting transfectant was cultured on a cover slip overnight, it was fixed with cold MeOH for 10 minutes. Next, it was allowed to react with CSLEX-1, diluted by a factor of 200, at room temperature for 1 hour and then reacted with secondary antibody (FITC-conjugated goat anti-mouse Ig(G+M), Jackson

Immuno Research Laboratories, Inc., West Grove, PA, USA), diluted by a factor of 100, for an additional hour. Dilution of antibody was performed with PBS containing 10% normal goat serum. After the reaction, the antibody was washed with PBS and the reaction product was then observed by a fluorescent microscope to obtain the fucosyltransferase type VII expression strain (CHO/FT7) that emitted fluorescence when stained.

Example B

Preparation of Cell Extract of CHO/FT7 Strain

After culturing CHO/FT7 cells, the cells were collected with a cell scraper and washed twice with PBS. The collected cells were ruptured by frozen liquefaction and then homogenized after suspending in 20 mM MOPS (pH 7.0). The homogenate was then centrifuged at 50,000 x g for 30 minutes and the membrane fraction was collected in the form of a pellet. This pellet was then suspended in 20 mM MOPS (pH 7.0) and 1% "TRITON X-100" at a protein concentration of 5 mg/ml. After the suspension was stirred at 4°C for 3 hours, it was centrifuged at 100,000 x g for 30 minutes. The resulting supernatant was used in the enzyme reaction in the form of solubilized fucosyltransferase type VII enzyme solution.

Example C

Assay of Activity of Fucosyltransferase Type VII

An enzyme reaction was carried out using fetuin (Sigma, St. Louis, MO, USA) as the substrate. 1.5 mg/ml of fetuin and the fucosyltransferase type VII enzyme extract were allowed to react at 37°C in 50 µl of 50 µM MPOS (pH 7.0), 3.2 µM [^{3}H] GDP-fucose (New England Nuclear, Boston, MA, USA), 10 mM L-fucose, 20 mM $MnCl_2$, and 5 mM ATP. Two hours later, 100 µl of reaction stopper (0.1 N HCl, 1% phosphotungustic acid) was added to precipitate the fetuin. Following precipitation, the fetuin

was collected on a Unifilter (Packard Instrument Company, Meriden, CT, USA) with a Cell Harvester (Packard Instrument Company) and dried overnight. 50 µl of Scintillator 0 was added to the dried Unifilter followed by measurement of the radioactivity incorporated in the fetuin using the Top Count (Packard Instrument Company). The results are shown in the following Table 1:

Table 1

Compound of Example No.	IC_{50} (µM)
46	537
47	674
50	216
57	264
61	310
71	2

Example D

Human P-selectin purification

Thirty units of outdated platelet concentrates (human platelet concentrates for transfusion which are beyond the expiration date defined by Japanese Red Cross) were washed three times with a buffer (pH=7.4) containing 150 mM NaCl, 10 mM Tris-HCl, 5 mM EDTA and 15% (v/v) acid/citrate/dextrose anticoagulant. Washed platelets were lysed with 150 ml of a buffer containing 150 mM NaCl, 10mM Tris-HCl, 1 mM benzamidine, 1mM PMSF, and 0.05% NaN3 (buffer C) containing 1% "TRITON X-100" (pH=7.4) in ice water. After ultracentrifugation at 80,000 x g for 60 minutes at 4°C, the supernatant was applied to a column of Sepharose CL-4B coupled with wheat germ agglutinin and recirculated for 4 hours at room temperature. After washing with 1000 ml of buffer C containing 0.1% "TRITON X-100" (pH=7.4), the bound materials were eluted with 100 ml of buffer

: containing 100 mM GlcNAc (pH=7.4). The eluate was applied to ı WGA-1 affinity column (10 ml of wet gel containing 10 mg of ıAb) and recirculated for 12 hours at room temperature. After ıashing with 1000 ml of buffer C containing 0.1% "TRITON X-100" ınd 0.5 M LiCl (pH=7.4), the bound protein was eluted with 100 ıl of buffer C containing 50 mM diethylamine (pH=11.5). The ɜluate was immediately neutralized with solid glycine. The ɜluate was concentrated by ultrafiltration using an Amicon 8050 ɜnd dialyzed against 150 mM NaCl and 10mM Tris-HCl containing ɔ.1% "TRITON X-100" (pH=7.4) and used as a P-selectin ɒreparation. The selectins are glycoproteins that initiate leukocyte adhesion to vascular endothelium and platelets in response to inflammatory stimuli.

Example E

HL-60 Cell Adhesion Assay

Human platelet P-selectin in HBSS (Hanks balanced Salt Solution) was coated directly on wells of 96-well microtiter plates at 4°C overnight (100µl/well). After coating, the plates were washed twice with HBSS, blocked with 300 µl of 1% FCS in HBSS for 2 hours at room temperature, and washed three times with HBSS.

Human HL-60 cells were maintained in RPMI-1640 containing 10% FCS. For adhesion assays, the cells were suspended at a concentration of 4 x 106 /ml in HBSS containing 1.26 mM Ca^{2+} and 0.81 mM Mg^{2+} plus 1% FCS (FCS/HBSS).

To determine whether a compound could inhibit HL-60 cell adhesion to immobilized P-selectin, 50 µl of serial dilutions of a compound in FCS/HBSS were preincubated with immobilized P-selectin for 15 minutes at 4°C. 50 µl of cell suspension were then added to the wells and incubated at room temperature for 20 minutes.

The wells were then filled with FCS/HBSS, sealed with acetate tape, and inverted for 10 minutes to separate unbound cells. The number of adherent cells was quantified using the myeloperoxidase activity of the cell.

With respect to the above adhesion assay, see the following publications:

(1) Ishiwata, N., et al., J. Biol. Chem., 269, 23708-23715, (1994)

(2) Ushiyama, S., et al., J. Biol. Chem., 268, 15229-15237, (1993).

The results of the HL-60 cell adhesion assay are set forth in the following Table 2.

Table 2

Effect on HL-60 Cell Adhesion to Immobilized P-Selectin

Compound of Example No.	% Inhibition IC_{50} (mg/ml)
7	1.2
24	1.5
25	1.8
32	3.3
35	1.9
43	0.5
46	0.6
48	2.2
52	2.0
54	1.7
55	0.9
57	0.6
61	0.5
71	1.4

Example F

ELISA Assay For Selectin Binding

ELISA assays for selectin binding and inhibition were performed as described in Foxall et al., (1992), "Three members of the selectin receptor family recognize a common carbohydrate epitop, the sialyl Lewis X oligosaccharide", J. Cell. Biol., 117, 895-902. Glycolipids dissolved in chloroform/methanol/water (4:8:3) that form the recognized surface were dried and reconstituted in 50% methanol/water at the desired concentrations. Fifty microliters were added to each Pro-Bind Assay Plates (Falcon, Becton Dickinson Labware, Lincoln Park, New Jersey (USA)) microliter wells and were allowed to dry. Adsorption efficiencies of a variety of negatively charged glycolipids have been determined (Blackburn et al., (1986), "Gangliosidessupport neural retina cell adhesion", J. Biol. Chem., 261, 2873-2881; Tyrrell et al., (1991), "Structural requirements for the carbohydrate ligand for E-selectin", Proc. Natl. Acad. Sci., 88, 10372-10376 were and found to be nearly identical, regardless of carbohydrate structure. Coated wells were washed with distilled water and blocked with 5% BSA in Dulbecco's phosphate-buffered saline (PBS) for 1 hour at room temperature. Plates were then washed three times with PBS. The following were added to PBS containing 1% BSA: (i) 1:1000 dilution of biotinylated goat F(ab') anti-human IgG Fc (Caltag, South San Francisco, CA, USA); (ii) 1:1000 dilution of alkaline phosphatase-streptavidin (Caltag); (iii) 100-300 ng/ml E-Selectin, L-Selectin or P-Selectin-IgG chimera. These reagents were allowed to form a complex for 15-30 minutes at room temperature before addition to coated wells (50 µl/well). Inhibitors or antibodies, when used, were added to the selectin complexes 45 minutes before transfer of the mixtures to coated wells. The selectin complexes were incubated in the wells for 45 minutes at 37°C, then washed three times with PBS, followed

by three washes with distilled water. The detection reagent, 1 mg/ml p-nitro-phenylphosphate in 1 M diethanolamine with 0.01% MgCl (pH 9.8), was added (50 µl/well) and the color developed for 30-60 minutes. Plates were read at 405 nm in a microliter plate reader (Molecular Devices, Menlo Park, CA, USA) IC_{50} values for inhibitors of cell adhesion were obtained by plotting the raw data (OD versus inhibitor concentration), then extrapolating from the OD value at 50% inhibition and estimating the corresponding inhibitor concentration. Each experiment was performed with n ≥ 3. The results are shown in the following Table 3.

TABLE 3

IC_{50} (mM)

Compound of Example No.	E	L	P
4	>1.0	0.114	0.081
5	>1.0	0.003	0.002
7	>1.0	0.106	0.007
12	>1.0	0.170	0.112
16	>1.0	<0.001	0.003
18	>1.0	0.035	0.046
19	>1.0	0.011	0.047
62(c)	>1.0	0.059	0.052
63	>1.0	0.015	0.002
77(b)	>1.0	0.080	0.013
77(c)	>1.0	0.240	0.110
82(c)	>1.0	0.100	0.017

Example H

Chronic Asthma Assay

Animals and Asthmatic Model

Male Hartley guinea pigs (Japan SLC. Shizuoka, Japan) weighing 350-400 g were raised at a temperature of 23 ± 1°C and humidity of 60 ± 5%. They were deprived of food for 1 day before the experiments.

The animals were sensitized with 0.5 ml of 5% ovalbumin subcutaneously and 0.5 ml intraperitoneally using the method

described by Engineer, D.M., Niedelhauser, U., Piper, P.J., Sirois, P., Release of mediators of anaphylaxis: Inhibition of prostaglandin synthesis and the modification of release of slow reacting substance of anaphylaxis and histamine, Br. J. Pharmacol., (1978), 62, 61. A booster injection was performed 7 days later. Seven or eight days after the booster injection, ovalbumin (10 mg/ml) was inhaled by a nebulizer undercover of an H1 antagonist, mepyramine (10 mg/kg, ip, -30 minutes). The duration of the antigen exposure was 3 minutes. The second challenge was performed 7 days later, and the guinea pigs were used 8 or 9 days after this.

Biphasic Bronchial Responses

As an index of bronchoconstriction, specific airway resistance (sRaw) was determined before and 0 to 6 hours after antigen inhalation by the method of Pennock, B.E., Cox, C.P., Rogers, R.M., Cain, W.A. and Wells, J.H., "A noninvasive technique for measurement of changes in specific airway resistance", J. Appl. Physiol., (1979), 46, 399 on a breath-by-breath basis in a double-chamber plethysmograph with a respiratory analyzer (Non-Invasive Model, Buxco Electronics, Inc., Sharon, CT) and data logger (Model OA-16, Buxco Electronics, Inc.).

ΔsRaw (% of baseline), an integral value taken from the

Example G

PAF-induced eosinophil homotypic aggregation

Preparation of guinea-pig eosinophils

Eosinophils were harvested from the peritoneal cavity of polymyxin B-treated guinea pigs according to the method described by Pincus S.H (1978, Production of eosinophil-rich guinea pig peritoneal exudates, Blood 52, 127-135). Male outbred guinea pigs were injected intraperitoneally with 1 mg of polymyxin B weekly for more than 5 weeks. At 48 hours after

the final injection, the peritoneal cavity was lavaged after exsanguination under ether anesthesia. The cells were washed twice by centrifugation and resuspended in 4 ml buffer (Eagle-MEM containing 10 mM HEPES). For purification of eosinophils, the peritoneal lavage fluid was overlaid on an equal volume of Ficoll-Paque (Pharmacia). The tubes were centrifuged at 150 xg for 20 min at room temperature, and the sediment (eosinophil-rich fraction) was washed twice the buffer.

Aggregation

Aggregation experiments were carried out with homocytometer. Briefly, guinea-pig eosinophils were resuspended (5×10^6 cells/ml) in Eagle-MEM buffer and aliquots (80 ml) of cells were dispended into siliconized tubes. The cells were preincubated for 5 min at 37 • • with drugs (10 ml), anti-L selectin antibody (MEL-14) or vehicle (10 ml), and then stimulated with 10 ml aliquots of PAF (final 10^{-5}M). Responses were allowed to develop for at least 30 min and the percent aggregation was calculated as described below;

percent aggregation=(1-B/A) x 100; where A is whole cell counts in tubes, and where B is whole total number of culusters of aggregated eosinophils consisted of more than two cells and single cells.

The inhibitory effects of the test compounds were calculated as follows;

percent inhibition = [1-(C-A)/(B-A)] x 100

A: percent aggregation of PAF-stimulated eosinophils pretreated with anti-L-selectin antibody (MEL-14, final 100 mg/ml).

B: percent aggregation of PAF-stimulated eosinophils pretreated with vehicle.

C: percent aggregation of PAF-stimulated eosinophils pretreated with test compounds.

Table 4

Compound of Example No.	Inhibition at 100µg/ml
102	77%
112	68%
114	68%
132	79%
136	72%
138	67%
146	62%

time-response curves, was used as an index of the intensity of bronchoconstriction. ΔsRaw values from 0 to 2 hours and in which sRaw returned to the baseline after the antigen challenge indicated IAR, and ΔsRaw values from 2 hours to 6 hours indicated LAR. The inhibitory effects of the test compounds were calculated as follows: inhibition (%) = (1-B/A) x 100; A: mean values of ΔsRaw in control animals; B:ΔsRaw values in test compound-treated animals.

Airway Hyperresponsiveness

Airway responsiveness was determined by measuring airway resistance to doubling the concentration of methacholine. As an index of bronchoconstriction to methacholine, respiratory resistance was automatically measured by a forced oscillation technique using Animal-asto (TMC-2100, Chest-MI, Japan) with a multi-nebulizer, based on the method of Mead, J., Control of Respiratory Frequency, J. Appl. Physiol., (1960), 73, 77. In brief, guinea pigs were placed inside a body plethysmograph, and a 30-Hz sine wave oscillation was applied to the animal body surface. The flow rate through the mask and the box pressure were measured by a differential pressure transducer. The 30-Hz components of a mask flow and a box pressure were extracted by a lock-in amplifier. The resistance was calculated by an analog computer according to the method of Hyatt, R.E., Zimmerman, J.R., Peters, G.M., Sullivan, W.J., Direct writeout of respiratory resistance, J. Appl. Physiol., (1970), 28, 675.

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Mask flow, body pressure and resistance were recorded using a multichannel polygraph recorder.

Methacholine (32 - 4096 µg/ml) or saline aerosol were generated using an ultrasonic nebulizer driven by compressed air. Saline was inhaled for 1 minute, and increasing concentrations of methacholine were inhaled for 1 minute each at intervals of 1 minute. The minimum provocative concentration of methacholine at which resistance exceeded 200% of the baseline value of individual animals was calculated and expressed as PC_{200} (µg/ml). PC_{200} values were determined 24 hours after antigen inhalation. The inhibitory effects of the test compounds were calculated as follows:

Percentage inhibition = [1-(C-A)/(B-A)] x 100

A: mean value of PC_{200} in normal animals

B: mean value of PC_{200} 24 hours after antigen challenge in control animals

C: PC_{200} 24 hours after antigen challenge in guinea pigs pretreated with a test compound.

Eosinophil Accumulation in BALF

Guinea pigs were anesthetized with pentobarbital (30 mg/kg, i.p.) before each bronchoalveolar lavage. The trachea was cannulated by a disposable intravenous catheter, 3 Fr size (ATOM Co, Tokyo, Japan), and the airway lumen was washed three times with an equal volume of 0.9% saline at 37°C (10 ml/kg). Typically, more than 75% of the fluid was recovered. The BALF collected from each animal was immediately placed in an ice bath and centrifuged (150 g for 10 minutes at 4°C). The cell pellets obtained by centrifugation of BALF were resuspended in 4 ml HBSS (Hank's balanced solution) and total cell counts were performed using a standard hemocytometer. Differential cell counts were performed on smears fixed in methanol and stained with Wright solution. A minimum of 500 cells per smear were

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counted by light microscopy under oil immersion (x1000). The proportion of each cell population was expressed as a percentage of total cells, and this ratio, together with the total cell count, was used to calculate the total number of each cell type.

The inhibitory effects of the test compounds were calculated as follows:

Percentage inhibition = [1-(C-A)/(B-A)] x 100

A: mean value of cell counts in BALF from normal animals

B: mean value of cell counts in BALF from guinea pigs 24 hours after antigen challenge

C: cell counts of BALF from guinea pigs pretreated with a test compound 24 hours after antigen challenge.

Example I

Acute Pulmonary Eosinophilia Assay Antigen-induced Eosinophil Accumulation

Animals and Asthmatic Model

Male Hartley guinea pigs (Japan SLC. Shizuoka, Japan) weighing 350-600 g were raised at a temperature of 23 ± 1°C and humidity in 60 ± 5%. They were deprived of food for 1 day before the experiment. The animals were sensitized with 0.5 ml of 5% ovalbumin subcutaneous and 0.5 ml intraperitoneal injection by the method described by Engineer et al., supra. A booster injection was performed 7 days later, and the guinea pigs were used 8 or 9 days after the final injection.

Eosinophil Accumulation

The animals were placed in a clear plastic chamber (41x41x50 cm) which was connected to the output of a supersonic wave nebulizer (NE-U11B, OMRON, Tokyo, Japan). All animals inhaled 10 µg/ml salbutamol, a β_2-adrenocepter agonist, for 5 minutes before antigen exposure. This treatment was necessary

to prevent acute fatal anaphylaxis. The duration of the antigen (ovalbumin: 10 mg/ml) exposure was 6 minutes.

Four hours after antigen challenge, the guinea pigs were anesthetized with pentobarbital (30 mg/kg, ip). The trachea was cannulated by a disposable intravenous catheter, 3 Fr size (ATOM Co, Tokyo, Japan), and the airway lumen was washed three times with equal portions of 0.9% saline (10 ml/kg). Typically, more than 75% of the fluid was recovered. The bronchoalveolar lavage fluid from each animal was centrifuged (150 g for 10 minutes at 4°C), the cell pellet was resuspended in 4 ml HBSS (Hank's balanced solution) and a total cell count was performed using a standard hemocytometer. Differential cell counts were done on smears fixed in methanol and stained with Wright solution. A minimum of 500 cells per smear were counted by light microscopy under oil immersion (x1000). The proportion of each cell population was expressed as a percentage of total cells, and this ratio, together with the total cell count, was used to calculate the total number of each cell type. The percentage inhibition obtained with the test compounds was calculated as follows:

Percentage inhibition = [1-(C-A)/(B-A] x 100

A: mean value of cell counts in bronchoalveolar lavage fluid from guinea pigs with inhaled saline

B: mean value of cell counts in bronchoalveolar lavage fluid from guinea pigs 4 hours after antigen challenge

C: cell counts of bronchoalveolar lavage fluid from guinea pigs pretreated with a test compound 4 hours after antigen challenge.

The present compounds showed excellent activity with respect of the tests set forth in Examples 89 and 90.

It will be appreciated that the instant specification is set forth by way of illustration and not limitation, and that various modifications and changes may be made without departure from the spirit and scope of the present invention.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

(ii) TITLE OF INVENTION: Aryl C-Glycoside Compound And Its Sulfate Form

(iii) NUMBER OF SEQUENCES: 2

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Frishauf, Holtz, Goodman, Langer & Chick, P.C.

(B) STREET: 767 Third Avenue

(C) CITY: New York

(D) STATE: New York

(E) COUNTRY: USA

(F) ZIP: 10017-2023

(v) COMPUTER READABLE FORM:

(A) MEDIUM DISKETTE: Floppy disk

(B) COMPUTER: IBM PC compatible

(C) OPERATING SYSTEM: PC-DOS/MS-DOS

(D) SOFTWARE: ASCII

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:

(B) FILING DATE:

(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER:

(B) FILING DATE:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Barth, Richard S.

(B) REGISTRATION NUMBER: 28,180

(C) REFERENCE/DOCKET NUMBER: 960059/HG

(ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: (212) 319-4900

(B) TELEFAX: (212) 319-5101

(C) TELEX: 236268

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS:

(D) TOPOLOGY:

(ii) MOLECULE TYPE: nucleic acid

(vi) ORIGINAL SOURCE: (A) ORGANISM:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GTGGATGAAT GCTGGGCACG G 21

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 base pairs

(B) TYPE: nucleic acid

(C) STR ANDEDNESS:

(D) TOPOLOGY:

(ii) MOLECULE TYPE: nucleic acid

(vi) ORIGINAL SOURCE:

(A) ORGANISM:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

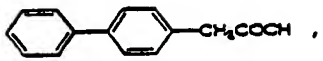
GATCTCAGGC CTGAAACCAA CCCT 24

Claims

1. An aryl C-glycoside compound comprising an aryl part and a glycosyl part, wherein the aryl part represents a phenyl acetic acid moiety which provides an anti-inflammation effect, which is unsubstituted or substituted with more than one 1'-glycosyl compound and the glycosyl part represents a natural or artificial monosaccharide having an α or β bond, or a disaccharide, a trisaccharide or a tetrasaccharide of said monosaccharide, said saccharides being unsubstituted or substituted by at least with a carboxyalkyl group or an acyl group;

or a sulfate ester thereof or a pharmaceutically acceptable salt thereof.

2. The aryl C-glycoside of claim 1, wherein the aryl part is selected from the group consisting of



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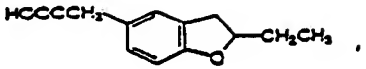

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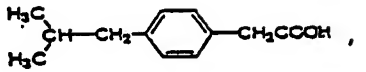

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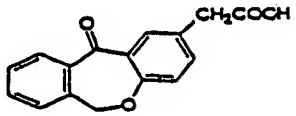

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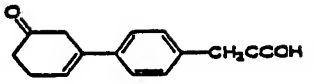

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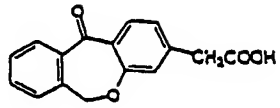
251



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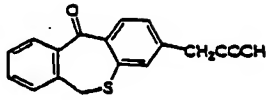

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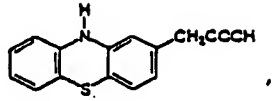

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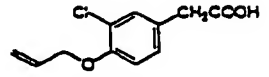

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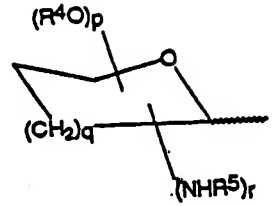
3. The aryl C-glycoside of claim 1, wherein the 1'-glucosyl part is a monosaccharide of the following formula (II):



(II)

wherein R^4 is a hydrogen atom, a carboxyalkyl group or an acyl group;

R^5 is a hydrogen atom or an acyl group;

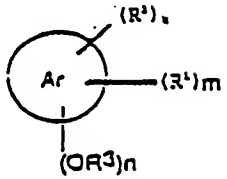
p is an integer of 1 to 5;

q is an integer of 1 or 2; and

252

r is 0 or 1.

4. An aryl C-glycoside of the following formula (I)



(I)

wherein R^1 is a saccharide which is a natural or artificial monosaccharide having an α or a β bond or a disaccharide, a trisaccharide or a tetrasaccharide of said monosaccharide, said saccharide being unsubstituted or substituted by at least with a carboxyalkyl group or an acyl group;

m is an integer of 1 to 4;

(Ar) is an aromatic or heterocyclic aromatic group;

R^2 is a hydrogen atom, a hydroxy group, an amino group, a halogen atom, a carboxy group, or a straight, branched or cyclic alkyl group which is unsubstituted or substituted with an oxo group, a hydroxy group, a carboxy group, a carboximide group, or a sulfonic acid group, or R^2 is cyclized with the (Ar) to form a condensed ring group;

k is an integer of 1 to 4, when k is 2 to 4, the atom or groups representing R^2 are the same or different;

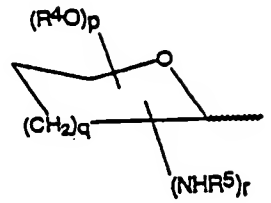
R^3 is a hydrogen atom, an alkyl group or an acyl group; and

n is an integer of 1 to 4;

or a sulfate ester thereof, or a pharmaceutically acceptable salt thereof.

5. The aryl C-glycoside of claim 4, wherein R^1 is a natural or artificial monosaccharide having an α or β bond, which is unsubstituted or substituted by a carboxylalkyl group or an acyl group.

6. The aryl C-glycoside of claim 4, wherein R^1 is a monosaccharide of the following formula (II):



(II)

wherein R^4 is a hydrogen atom, a carboxyalkyl, group or an acyl group;

R^5 is a hydrogen atom or an acyl group;

p is an integer of I to 5;

q is an integer of 1 or 2; and

r is 0 or 1.

7. The aryl C-glycoside of claim 4, wherein R^1 is a natural monosaccharide having an α bond or a β bond.

8. The aryl C-glycoside of claim 4, wherein R^1 is selected from the group consisting of glucose, glucosamine, galactose, galactosamine, fucose, mannose, sialic acid, ribose, rhamnose, xylose, arabinose, lyxose, 2-deoxygalactose, 2-deoxyglucose, fructose, sorbose, allose, aitrose, talose, tagatose, glucronic acid, galacturonic acid, lactose, maltose, cellobiose, gentiobiose, melibiose, maltotriose and maltotetraose.

9. The aryl C-glycoside of claim 4, wherein (Ar) is an aromatic having 6 to 18 carbon atoms or a 5 to 14-membered

aromatic heterocyclic having 1 to 3 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen.

10. The aryl C-glycoside of claim 4, wherein Ar is an aromatic group having 6 to 12 carbon atoms.

11. The aryl C-glycoside of claim 5, wherein Ar is an aromatic group having 6 to 12 carbon atoms.

12. The aryl C-glycoside of claim 6, wherein Ar is an aromatic group of 6 to 12 carbon atoms.

13. The aryl C-glycoside of claim 4, wherein Ar is selected from the group consisting of a benzene ring, a naphthalene ring, an anthracene ring, a phenanthrene ring, an indene ring, a fluorene ring, a stilbene ring, an indane ring, a 1,2,3,4-tetrahydronaphthalene ring, a 9,10-dihydroanthracene ring, a biphenyl, a diphenylmethane, a diphenylethane and a diphenyl ether.

14. The aryl C-glycoside of claim 5, wherein Ar is selected from the group consisting of a benzene ring, a naphthalene ring, an anthracene ring, a phenanthrene ring, an indene ring, a fluorene ring, a stilbene ring, an indane ring, a 1,2,3,4-tetrahydronaphthalene ring, a 9,10-dihydroanthracene ring, a biphenyl, a diphenylmethane, a diphenylethane and a diphenyl ether.

15. The aryl C-glycoside of claim 6, wherein Ar is selected from the group consisting of a benzene ring, a naphthalene ring, an anthracene ring, a phenanthrene ring, an indene ring, a fluorene ring, a stilbene ring, an indane ring,

a 1,2,3,4-tetrahydronaphthalene ring, a 9,10-dihydroanthracene ring, a biphenyl, a diphenylmethane, a diphenylethane and a diphenyl ether.

16. The aryl C-glycoside of claim 8, wherein Ar is selected from the group consisting of benzene, naphthalene, anthracene, phenanthrene, indene, fluorene, stilbene, indan, 1,2,3,4-tetrahydronaphthalene, 9,10-dihydroanthracene, 9,10-dihydrophenanthrene, estradiol, biphenyl, diphenylmethane, diphenylethane, diphenyl ether, xanthene, furan, benzofuran, dibenzofuran, chromanone, flavone, flavonone, thiopene, thianaphthene, pyrrole, pyrazole, imidazole, oxazole, isoxazole, isothiazole, thiazole, 1,2,3-oxadiazole, triazole, tetrazole, thiadiazole, pyridine, pyridazine, pyrimidine, purazine, indole, indazole, purine, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbozole, carboline, phenanthridine and acridine.

17. The aryl C-glycoside of claim 4, wherein R^2 is a straight, branched or cyclic alkyl group which is unsubstituted or is substituted by at least with an oxo group, a hydroxy group, a carboxy group or a sulfonic acid group, and when R' represents a straight, branched or cyclic alkyl group, which optionally is cyclized with the Ar group to a condensed group.

18. The aryl C-glycoside of claim 4, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, which optionally is cyclized with the Ar group to a condensed ring group.

19. The aryl C-glycoside of claim 5, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, which optionally is cyclized with the Ar group to a condensed group.

20. The aryl C-glycoside of claim 6, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, which optionally is cyclized with the Ar group to a condensed ring group.

21. The aryl C-glycoside of claim 10, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, which optionally is cyclized with the Ar group to a condensed ring group.

22. The aryl C-glycoside of claim 11, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, which optionally is cyclized with the Ar group to a condensed ring group.

23. The aryl C-glycoside of claim 12, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group, which optionally is cyclized with the Ar group to a condensed ring group.

24. The aryl C-glycoside of claim 4, wherein R^2 is a straight or branched alkyl group which is substituted by at least with a carboxy group or a sulfonic acid group.

25. The aryl C-glycoside of claim 4, wherein R^2 is a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a sulfonic acid group.

26. The aryl C-glycoside of claim 5, wherein R^2 is a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a sulfonic acid group.

27. The aryl C-glycoside of claim 6, wherein R^2 is a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a sulfonic acid group.

28. The aryl C-glycoside of claim 10, wherein R^2 is a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a sulfonic acid group.

29. The aryl C-glycoside of claim 11, wherein R^2 is a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a sulfonic acid group.

30. The aryl C-glycoside of claim 12, wherein R^2 is a cyclic alkyl group which is substituted by at least with an oxo group, a carboxy group or a sulfonic acid group.

31. The aryl C-glycoside of claim 4, wherein m is an integer of 1 to 2.

32. The aryl C-glycoside of claim 4, wherein m is 1.

33. The aryl C-glycoside of claim 4, wherein k is 1 or 2 and when k is not 1, R^2 is the same or different.

34. The aryl C-glycoside of claim 4, wherein R^3 is a hydrogen atom, a C_1-C_{10} alkyl group or a C_1-C_{10} acyl group.

35. The aryl C-glycoside of claim 4, R^3 is a hydrogen atom or a C_1-C_{10} alkyl group.

36. The aryl C-glycoside of claim 4, n is an integer of 1 to 2.

37. The aryl C-glycoside of claim 4, which is [2-(β-L-fucopyranosyl)-3,4,5-trimethoxyphenyl]acetic acid.

38. The aryl C-glycoside of claim 4, which is [3-(β-L-fucopyranosyl)-4-methoxyphenyl]acetic acid.

39. The aryl C-glycoside of claim 4, which is 1-(3-β-L-fucopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid.

40. The aryl C-glycoside of claim 4, which is [3-(β-L-fucopyranosyl)-4-methoxyphenyl]butyric acid.

41. The aryl C-glycoside of claim 4, which is 1-[3-(β-D-galactopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid.

42. The aryl C-glycoside of claim 4, which is 1-[4-methoxy-3-(β-L-rhamnopyranosyl)phenyl]cyclohexanecarboxylic acid.

43. The aryl C-glycoside of claim 4, which is 1-[4-methoxy-3-(β-D-xylopyranosyl)phenyl]cyclohexanecarboxylic acid.

44. The aryl C-glycoside of claim 4, which is 6-(β-L-fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)benzene.

45. The aryl C-glycoside of claim 4, which is 1-(β-L-fucopyranosyl)-2,6-dimethoxy-5(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid)naphthalene.

46. The aryl C-glycoside of claim 4, which is 2,6-dimethoxy-1-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)-5-(sodium β-L-fucopyranosyl 2,3,4-trisulfate)naphthalene.

47. A pharmaceutical composition for treating or preventing an inflammatory disease, an autoimmune disease, an infection, a cancer, a reperfusion disorder, a thrombosis, an ulcer, a wound or osteoporosis comprising a pharmaceutically effective amount of the aryl C-glycoside of claim 1 in admixture with a pharmaceutically acceptable excipient.

48. The pharmaceutical composition of claim 47, wherein the aryl C-glycoside is selected from the group consisting of

[2-(β-L-fucopyranosyl)-3,4,5-trimethoxyphenyl] acetic acid,

[3-(β-L-fucopyranosyl)-4-methoxyphenyl]acetic acid,

1-[3-β-L-fucopyranosyl)-4-methoxyphenyl] cyclohexanecarboxylic acid,

[3-(β-L-fucopyranosyl)-4-methoxyphenyl]butyric acid,

1-[3-(β-D-galactopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid,

1-[4-methoxy-3-(β-L-rhamnopyranosyl)phenyl]cyclohexanecarboxylic acid,

1-[4-methoxy-3-(β-D-xylopyranosyl]phenyl]cyclohexanecarboxylic acid,

6-(β-L-fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-glycero-α-D-galacto-2-nonulopyranosylonic acid)benzene,

1-(β-L-fucopyranosyl)-2,6-dimethoxy-5(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) naphthalene, and

2,6-dimethoxy-1-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)-5-(sodium β-L-fucopyranosyl 2,3,4-trisulfate) naphthalene.

49. A method for treating an inflammatory disease, an autoimmune disease, an infection, a cancer, a reperfusion disorder, a thrombosis, an ulcer, a wound or osteoporosis in a mammal comprising administering to a mammal a pharmaceutically effective amount of the aryl C-glycoside of claim 1, either alone, or in admixture with a pharmaceutically acceptable excipient.

50. The method of claim 49, wherein the aryl C-glycoside is selected from the group consisting of

[2-(β-L-fucopyranosyl)-3,4,5-trimethoxyphenyl]acetic acid,

[3-(β-L-fucopyranosyl)-4-methoxyphenyl]acetic acid,

1-(3-β-L-fucopyranosyl)-4-methoxyphenyl] cyclohexanecarboxylic acid,

[3-(β-L-fucopyranosyl)-4-methoxyphenyl]butyric acid,

1-[3-(β-D-galactopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid,

1-[4-methoxy-3-(β-L-rhamnopyranosyl)phenyl]cyclohexanecarboxylic acid,

1-[4-methoxy-3-(β-D-xylopyranosyl)phenyl]cyclohexanecarboxylic acid,

6-(β-L-fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) benzene,

1-(β-L-fucopyranosyl)-2,6-dimethoxy-5(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) naphthalene, and

2,6-dimethoxy-1-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)-5-(sodium β-L-fucopyranosyl 2,3,4-trisulfate) naphthalene.

51. A method for preventing an inflammatory disease, an autoimmune disease, an infection, a cancer, a reperfusion disorder, a thrombosis, an ulcer or osteoporosis in a mammal comprising administering to a mammal a pharmaceutically effective amount of the aryl C-glycoside of claim 1, either alone, or in admixture with a pharmaceutically acceptable excipient.

52. The method of claim 51, wherein the aryl C-glycoside is selected from the group consisting of

[2-(β-L-fucopyranosyl)-3,4,5-trimethoxyphenyl]acetic acid,

[3-(β-L-fucopyranosyl)-4-methoxyphenyl]acetic acid,

1-[3-β-L-fucopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid,

[3-(β-L-fucopyranosyl)-4-methoxyphenyl]butyric acid,

1-[3-(β-D-galactopyranosyl)-4-methoxyphenyl]cyclohexanecarboxylic acid,

1-[4-methoxy-3-(β-L-rhamnopyranosyl)phenyl]cyclohexanecarboxylic acid,

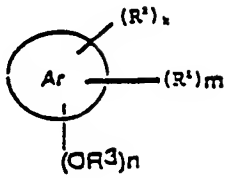
1-[4-methoxy-3-(β-D-xylopyranosyl)phenyl]cyclohexanecarboxylic acid,

6-(β-L-fucopyranosyl)-1,3-dimethoxy-4-(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) benzene,

1-(β-L-fucopyranosyl)-2,6-dimethoxy-5(5-acetamido-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonic acid) naphthalene, and

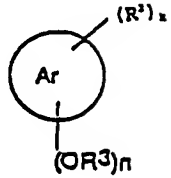
2,6-dimethoxy-1-(sodium β-D-galactopyranosyl 2,3,4,6-tetrasulfate)-5-(sodium β-L-fucopyranosyl 2,3,4-trisulfate) naphthalene.

53. A process for the preparation of a compound of the following formula (I):



(I)

in which R^1, R^2, R^3, (Ar) , k, n and m are as defined in claim 5, which process comprises reacting a compound of the following formula (III):



(III)

in which R^2, R^3, (Ar), k and n are as defined in claim 5, with a compound of the following formula (IV):

$$R^1\text{-}X \qquad \text{(IV)}$$

wherein R^1 is as defined in claim 5 and X is a leaving group,

in the presence of a mixed catalyst of at least one Lewis acid and at least one silver or mercury salt of trifluoromethane sulfonic acid or trifluoroacetic acid.

54. The method of claim 53, wherein the Lewis acid is selected from the group consisting of tin tetrachloride and gallium tetrachloride.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 98/00701

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07H7/04 A61K31/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 444 050 A (KOGAN TIMOTHY P ET AL) 22 August 1995 see the whole document ---	1-24, 31-36, 47-52
X	BE 886 879 A (KUREHA CHEMICAL IND CO LTD) 24 June 1981 see the whole document ---	1,47-52
X	B.DUPRE ET AL.: "Glycomimetic Selectin Inhibitors (alpha-D-mannopyranosyloxy)methylbiphenyls ." BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 6, no. 5, 1996, pages 569-572, XP002065252 see the whole document --- -/--	1-3

[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents :
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 May 1998	19. 06. 1998
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Scott, J

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INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 98/00701

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M.USHIYAMA ET AL.: "Studies on Plant Tissue Culture. Part 60. Biotransformation of Aromatic Carboxylic Acids by Root Culture of Panax Ginseng." PHYTOCHEMISTRY, vol. 28, no. 7, 1989, pages 1859-1869, XP002065253 see the whole document ---	1-3
X	D.DERRIEN ET AL.: "Muramyl Dipeptide Bound to Poly-L-Lysine Substituted with Mannose and Glucosyl Residues as Macrophage Activators." GLYCOCONJUGATE JOURNAL , vol. 6, no. 2, 1989, pages 241-255, XP002065254 see the whole document ---	1-3
X	J.DAI ET AL.: "Studies on the Indonesian Medicinal Plants. Part 3. Phenylacetic Acid Derivatives and a Thioamide Glycoside from Entada Phaseolides." PHYTOCHEMISTRY, vol. 30, no. 11, 1991, pages 3749-3752, XP002065255 see the whole document ---	1-3, 47-52
X	A.K.BARUS ET AL.: "Phaseoloidin, a Homogentisic Acid Glucoside from Estada phaseoloides" PHYTOCHEMISTRY , vol. 27, no. 10, 1988, pages 3259-3261, XP002065256 see the whole document ---	1-24
X	CHEMICAL ABSTRACTS, vol. 59, no. 3, 5 August 1963 Columbus, Ohio, US; abstract no. 3114a, S.TOMINO ET AL.: "Occurrence of (3,4-dihydroxyphenyl)acetic Acid Glucoside in Abdomen of Female Locust, Locust Migratoria." column 1; XP002065257 see abstract & EXPERIMENTIA, vol. 19, 1963, pages 231-232, ---	1-24
P,X	WO 97 01335 A (TEXAS BIOTECHNOLOGY CORP ;KOGAN TIMOTHY P (US); DUPRE BRIAN (US);) 16 January 1997 see the whole document -----	1-24, 31-36, 47-52

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No. PCT/US 98/00701

x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

s International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

[X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 49-52 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

[X] Claims Nos.: 1 partially
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

[ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

e International Searching Authority found multiple inventions in this international application, as follows:

[ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

[ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

[ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

[ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

emark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

rm PCT/ISA/210 (continuation of first sheet (1)) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 98/00701

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: 1 partially

In view of the large number of compounds, which are defined by the general definition in the independent claims, the search had to be restricted for economic reasons. Moreover, there are a multiplicity of clarity problems, and inconsistencies between the claims and examples. Thus the search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application. (see Guidelines, Chapter III, paragraph 2.3). More specifically, the search has been based mainly on the more clearly defined claims, 2-4.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter nal Application No
PCT/US 98/00701

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